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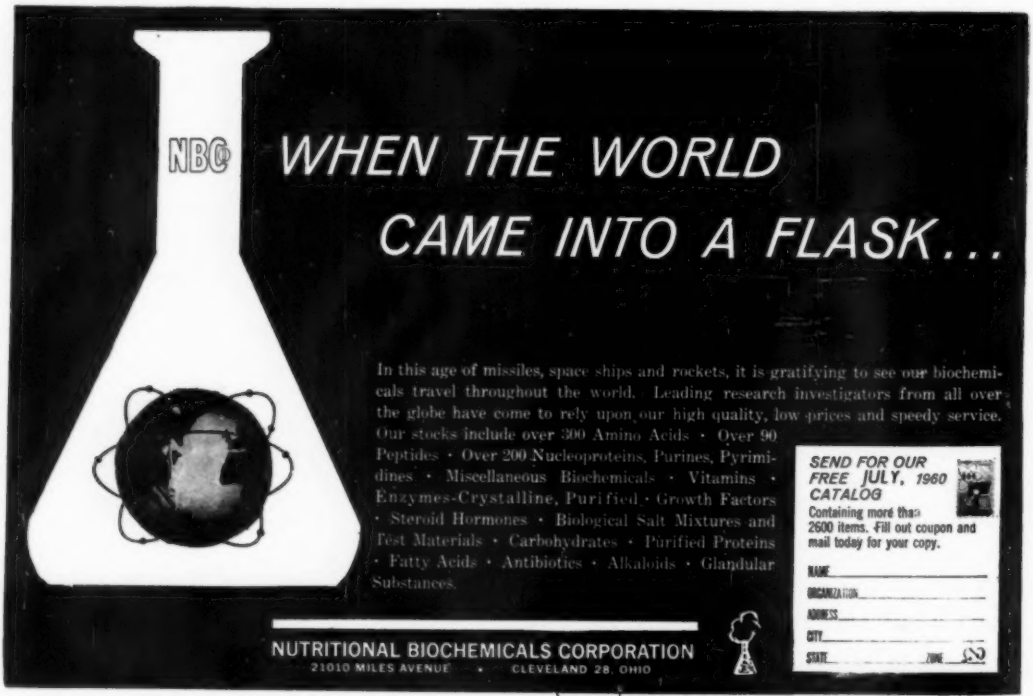
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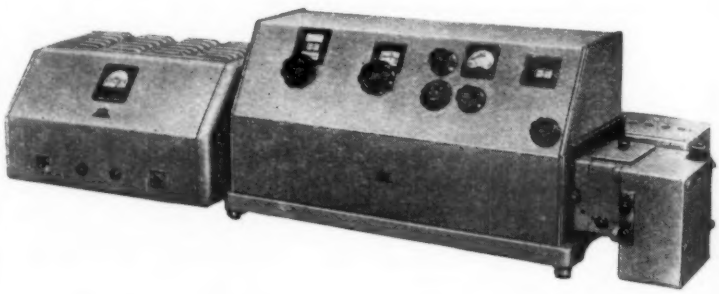

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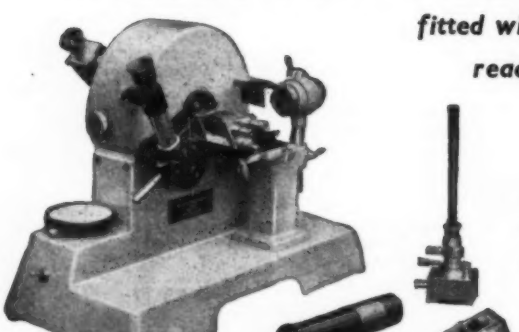

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THE LEARNED SOCIETY, THE ARTS AND THE SCIENCES

"IT is the duty of the Royal Society", said Sir Cyril Hinshelwood, in concluding his tercentenary address, "to maintain within the larger community the smaller one in which creative activity can flourish. Its members owe a multiplicity of loyalties, none of which can be fulfilled without the others: to mankind in general, to their native land, and to the Royal Society itself". "That is not all", he added, "for there are communities in time as well as in space, and the most original minds, in some sense isolated in all contemporary groupings, find their true affinities in continuing the sequence of their predecessors, and their fulfilment only in their successors".

In this concluding part of his address, Sir Cyril had been discussing the role of the scientific society in the world of to-day, and more especially its bearing on the relation of the individual to the community. The great movements of thought, he pointed out, and even the lesser ones of whim and fashion, spread from leaders, and only minorities in general exercise an independent taste and judgment or produce original thought. The propagation of an idea demands the right conjunction of unknown human factors, but even when these are propitious nothing will initiate the change save the operation of a minority small enough to defy statistical calculations.

While the majority and the minority are thus generally mutually dependent, in scientific investigations the lavish material ways and means needed, particularly the further knowledge advances, make the individual in isolation, except under rare conditions, correspondingly impotent. The community as a social and political whole cannot be expected, however, to possess the detailed understanding to support him, and with the tremendous issues at stake to-day, it is necessary to create, to mediate between the individual and the major group, a specialized minor community, large enough to command prestige and confidence, but with membership limited to those who put the claims of knowledge first. This is the part that the scientific society and academy, rather than some government institution or the universities, have to play, and Sir Cyril sees them as providing several vital things that neither government nor industry can provide so well. Sir Cyril instances non-commercial periodicals for the publication of discoveries, a measure of financial support for ideas still too embryonic to be of immediately obvious practical application, the mutual stimulus of association and discussion and the immaterial reward of honour for intellectual achievements.

If an academy maintains high standards of unquestioned impartiality, it sets the tone throughout the scientific community and exerts its influence far beyond the confines of the learned world. When the closest connexions with government organizations or industry are maintained, the professional men of science hear of the needs of the State and of industry, and these in their turn are irrigated by the currents of scientific thought. The process of communication of ideas, Sir Cyril rightly stressed, is not something purely mechanical but rather a sensitive nervous mechanism endowing the community which possesses it with capacities and potentialities realizable in no other way. The subtle co-ordinating action of an academy, he pointed out, can no more be replaced by a bureaucratic organization or a system of economic incentives and deterrents than the intrically evolved biological controls of a living organism can be replaced by widely devised mechanical appliances.

Sir Cyril Hinshelwood's remarks deserve to be deeply pondered by scientists and technologists both in relation to the scientific society and to the professional association. It is clear that both have a part to play in establishing the most effective conditions of communication and for the functioning of creative thought and work, and perhaps more especially in respect to the professional association. It is almost a generation since A. M. Carr-Saunders and P. A. Wilson published their study of the professions, and apart from the many changes in the organization of the professions, the time is ripe for a further critical examination of the functions of the professional, as well as of the scientific and learned, society in the world of to-day, and Sir Cyril's address challenges the creative thinking that is required. His comments indicate very clearly that the failure of some professional organizations to take clear decisions about individual and corporate membership may well prejudice the effectiveness with which they can serve the community as a whole.

The mutual stimulus of association and discussion is not, however, limited to the scientific society or academy as such. It can equally be carried out by a body in which the scientist and the non-scientist are brought together, as in the Manchester Literary and Philosophical Society, and in respect of promoting public understanding and creating the awareness of what is needed to support scientific activity, it may sometimes function more effectively than the purely scientific society. That Society has moved to its new buildings on the site of the premises which were destroyed by bombing in December 1940, in the hope that it may be a meeting place for people in Manchester who are interested in different aspects of the arts, science, commerce and industry. Quite apart from the fact that its own membership offers possibilities of wider contacts than the University itself could hope to provide even if not departmentalized, other societies in the city are already

arranging to use the new premises for their meetings, and there is some reason to hope the Society and its buildings may once again become the centre of Manchester's intellectual life.

Whether in the specialized scientific society or academy or in the more general society as exemplified by the Manchester Literary and Philosophical Society, this question of communication is all-important. What is needed above all is ease of communication across not merely the departments or disciplines of particular branches of science both within a university or academy and between the sciences generally and other fields of human endeavour. In addressing the Manchester Society, when he formally opened its new premises in September, Sir Cyril did not return to his earlier theme of the specific role of the learned society in the world of to-day, but he boldly challenged as artificial some of the distinctions between the arts and the sciences. He did not entirely accept as valid Sir Charles Snow's picture of the two cultures, and much that he said was not simply an eloquent plea to abolish some of the conventional distinctions between the arts and the sciences and to concentrate rather on what they had in common, but was a major contribution to the debate on general education and the education of the scientist in particular which had been a feature of the recent meeting of the British Association at Cardiff.

Prof. A. H. Cottrell, however, in a talk "Scientists : Solo or Concerted ?" broadcast in the Third Programme and printed in *The Listener* of September 15, dealt more specifically with this theme of the individual or the creative minority and the relation of individual or minority to the majority of the community in which they live, from which Sir Cyril Hinshelwood had originally approached the question of the scientific academy. Emphasizing how misleading can be the popular image of the solitary scientist withdrawn from the world, Prof. Cottrell pointed out that the scientist, however remote he may seem, is always bound closely to the scientific life around him. He cannot work in a vacuum, but has to take the ideas and problems as they exist among his fellows, transmute them in his own personal way and then bring them back as offerings to the community.

Prof. Cottrell's analysis of the way science advances is worth considering from this point of view of the function of the scientific or learned society. All scientists and technologists, he points out, are users of what has gone before them. At any instance there is a narrow frontier dividing what has gone before from the problems still to be solved, and while this frontier is occasionally stationary where it runs up against one of the big problems of science, for the most part it is steadily moving forward ; and keeping in touch with its position from day to day, even on a narrow sector, has become surprisingly difficult. In Prof. Cottrell's view, it is the main problem that the modern scientist has to face in his own work, and finding it exactly is half the battle in modern research. If the scientist does not find it, he is in danger either of being too timid and wasting his talents on a stale problem or of being too bold and futilely attempting the impossible. If, however, he can pin-point its position really well, deciding the next step forward and how to make it is often surprisingly easy.

Prof. Cottrell's own deduction from the effect of this principle on the pattern of scientific research itself, and the consequent emphasis on meeting as many people working in your own field as possible and meeting them as often as possible, is that where this cannot be done every day in a great laboratory, the need should be met in a scientific conference. His emphasis, moreover, is on the informal contacts and discussions at such conferences, when proceedings in any event are often very belatedly imperfectly reported, and his address lends no support to any proposal for elaborate mechanical means of indexing or recording their proceedings. He recognizes, in fact, that the real value of such conferences is derived from personal participation, and nothing can replace this.

Here, like Sir Cyril Hinshelwood, Prof. Cottrell is emphasizing the dependence of creative work on human qualities—boldness, conservatism, originality —that run through the fabric of all human endeavours, and to his mind the big projects and great laboratories are gradually leading to a new kind of creativity in science. By pooling their individual talents and efforts in a common purpose the members of such organizations are able to attempt new ventures with a boldness and on a scale far beyond the scope of the individual, and he compares the work of many modern laboratories in science with the collective creativity involved in the production of an opera or ballet. In some parts of science it has, of course, not yet become necessary to work in these large groups, but even so, the large laboratory offers advantages in keeping in touch with the frontier and in the stimulating company of one's colleagues. In nuclear physics, however, in radio astronomy, nuclear energy and aeronautical research, the equipment is so large and costly that there is no alternative.

Here again, Prof. Cottrell's thought seems to run with that of Sir Cyril's, and he suggests, indeed, that the arts have something to teach science in the organization of large-scale scientific research and how best to encourage the delicate but all-important balance between individual creative research and collective team-work. There are questions here of education on which Prof. Cottrell just touches, but it should be clear from his remarks how important a part the scientific society or academy has to play in the advancement of modern science. It will not indeed eliminate the need for the scientific conference, particularly at the international level, and it can play a useful part in promoting the organization of such conferences where required. Its real work, however, lies in the fostering of regular and easy and informal contacts and discussions, not simply between specialists, but across the different disciplines. Moreover, Sir Cyril Hinshelwood and Prof. Cottrell agree in recognizing the value of such contacts and discussions not merely within the

sciences but also across the boundaries of science and the arts. Societies like the Manchester Literary and Philosophical Society which seek to bring the scientist into closer and regular touch with those who work in different fields of art may well have a large contribution to make in stimulating creative thought and the new studies which are required to solve some of the major problems of the organization and administration of science itself, quite apart from the value of such contacts stimulating a fresh approach to some problems of science itself. Moreover, such societies assuredly have their part to play in the task of public education, of promoting the general understanding of the nature of science and the way it works and advances, that become more and more essential as the demands of science on the public purse extend.

For all such reasons it is to be hoped that the Literary and Philosophical Society in Manchester and kindred societies throughout Britain and elsewhere, no less than learned, scientific and professional societies generally, will respond to Sir Cyril's challenge to the Manchester Society and grasp their opportunities with boldness, with vision and with imagination.

EDMUND HUSSERL: 1859-1959

Edmund Husserl 1859–1959

Recueil Commémoratif publié a l'Occasion du Centenaire de la Naissance du Philosophe. (Phænomenologia, Vol. 4.) Pp. xi+306. (La Haye: Martinus Nijhoff, 1959.) 20 guilders.

THE year 1859 in which Edmund Husserl was born was indeed a landmark in the progress of European learning. It claimed also John Dewey, Samuel Alexander and Henry Bergson. As if that were not enough, in that same year Darwin's "Origin of Species" and Marx's "Critique" made their appearance. The passage of time was in fact to show that Husserl and Alexander both died in 1938. The present volume, beautifully printed and set out, was issued as a centenary collection in honour of the master of phenomenology. The twenty-five contributors, as one would expect, are leaders and critics in that branch of philosophy, and they write, for the most part, in their own languages, namely, English, French, German and Italian. Yet these pages are a typically 'overseas' assemblage; not one of the distinguished authors comes from Great Britain. In his lifetime particularly, Husserl's force was a Continental radiation having as it were secondary foci in the United States which have sharpened with the years and yielded him praise. But, nearer home, anyone who has visited the Archives at Louvain will read Prof. van Breda's paper in this book with particular pleasure. It is outstanding for its scholarship, sympathy and charity. Possibly not too well known is the fact that the savants there assumed the responsibility not only of safe custody, but also the task of transcribing (from Husserl's shorthand) and editing the mass of material which the late Frau Husserl had been able to deliver into their hands, and thus to save from the ravages of Hitler's *Reich*. As Prof. van Breda modestly remarks, Germany has gained a little intellectual territory in the process, a scholar's embassy on Belgian soil.

But this is only the result of something that was afoot some sixty-odd years ago. Husserl's mental strife was intense: he was able (and this was the operative part of the performance) to share it with his students, and literally to compel them to labour too. Stiff and formal—not unlike Max Planck—in his university lecturing, he was creative to a high degree in his seminars. All this was to one purpose, to obtain the greatest possible rigour (in theory, a pre-suppositionless philosophy), and to ask the right questions. Husserl was an artist in the shades of meaning, and his small audiences instinctively sensed his deft use of word and phrase. Of course, such a professor–pupil relationship, almost medieval in its fervour, would be unthinkable to-day with our crowded class-rooms and tight schedules. This book is worth reading on that score alone, to catch a glimpse of the kind of detachment necessary to become an epistemologist of stature. Husserl was a great enough man to reveal to his hearers much of his own early confusions, and how he escaped from them to do battle with psychologism, that is, the subtle intrusion of psychological elements into purely logical processes. Moreover, it should not be forgotten that he came to mental manhood as a pupil of the great Weierstrass, with a dissertation on the calculus of variations (1882), which apparently was never printed. In the publication now under review the reader is presented with a full bibliography, and a worthy reproduction of the drawing of the master by Rudolf Stumpf.

Husserl's attempt to use phenomenological methods in the sphere of social science was scarcely a success, if judged in relation to any form of transcendental theory of knowledge. But he achieved an advance; if one admits the value of philosophical anthropology as at least a worth-while development of the problems of the living world. Even though much of his work in this direction was contained within the restricted field of 'reduction' or 'bracketing'—corresponding to a suspension of judgment—yet he established a vital principle in his emphasis on the place of the natural attitude. The empirical type of sociology has much to learn from this, more particularly when one recollects how hard Husserl strove to practise what he preached. Those who enjoyed the intimacy of his friendship, and accompanied him on his 'philosophical walks' at Freiburg, must have become convinced that the peripatetic schools of the Golden Age at Athens must surely have come to life again. But Husserl could be very lengthy: it was not uncommon for him to think aloud, without notes of any kind, for a couple of hours on end, an ordeal which his listeners not only survived but even enjoyed. They were there *d'assister* at the birth of ideas, and they had their reward.

An element of paradox seems inseparable from much German thought. It is displayed here in Husserl's scientific philosophy as a free gift to those who would divest any theory of knowledge of its scientific content. He fought against naturalism only to help it on to its feet. In broad outline, Husserl shares with Sören Kierkegaard, Karl Barth, and Rudolf Otto the tendency to stress the 'wholly other'. In England we do not do this: our urge to find a middle way carries us in the opposite direction. Yet there is to-day a movement towards subjectivity, not in the mathematical sciences, but in biological

studies, which may well herald the advent of biophysics as the leading discipline in future experimental philosophy.

The chapters of this admirable book, each one by an acknowledged authority on his own ground, are written to survey a wide field: reminiscent, biographical, epistemological, psychological, and experiential. The late Dr. Alfred Schutz, one of the contributors, met Edmund Husserl many times during the nineteen-thirties in Freiburg, Vienna, or Prague, and sums up the impression that was universal, when the name of the master of phenomenology was mentioned, in just two words, "*Ecce philosophus*".

F. I. G. Rawlins

PRODUCTION AND PROCESSING OF URANIUM

Uranium Production Technology

Edited by C. D. Harrington and A. E. Ruehle. Pp. xii+579. (Princeton, N.J., and London: D. Van Nostrand Company, Inc., 1959.) 131*s.* 6*d.* net.

THIS book is the first comprehensive compilation of the technology of uranium production. The material for the book was prepared by the technical personnel of the Uranium Division of Mallinckrodt Chemical Works, under the direction and guidance of the United States Atomic Energy Commission's Division of Information Services. The Commission recently declassified virtually all the significant features of the technology, thus making possible the publication of the book.

For the benefit of the industrial chemist, the production of pure uranium from the ore concentrate is described in considerable detail both in regard to the plant and to the chemistry of the processes involved. Plant for both batch and continuous processes is described, and the accounts of advanced methods, such as ion exchange and fluidized bed techniques for the manufacture of both uranium tetrafluoride and hexafluoride, are of special interest. It is apparent that very little information has been withheld, and cost figures for many of the processes are included.

For the metallurgist and the engineer there are excellent chapters dealing with the vacuum casting and subsequent forming of the uranium metal, and again considerable detail of the plant is given.

Chapter 10 is worthy of special mention and deals with the physical metallurgy of uranium related directly to the problems of metal production and fabrication. The structure in terms of the allotropic forms of uranium, the response to heat treatment and the degree to which the grain size may be controlled are all discussed. Lists of the usual mechanical properties, showing the effect of temperature, are given, and the final section reviews mechanisms of alloy formation and shows the effects of additions on the physical properties, structure and mechanical properties. The photomicrographs showing the structure of uranium and of typical inclusions are particularly useful.

British experience of fabricating uranium metal by methods other than casting and machining is relatively limited. The next three chapters, dealing with forging, extrusion and rolling, might therefore have been expected to be of especial interest. In fact they are just a little disappointing—particularly that on extrusion—and it is difficult to believe that we are being given an adequate account of the fairly extensive body of American knowledge on these aspects. An additional chapter on fabricating high-uranium alloys gives some useful basic data; this chapter also has a very good bibliography.

The final chapter is devoted to health hazard control and gives an extensive review of this particularly important aspect of uranium processing. Shielding against beta and gamma radiation is described, and useful guidance on the methods available for dust control is given.

Few criticisms can be made of the book, and these are mainly minor ones. Its pages include a wealth of information on uranium production and processing. Extensive use is made of diagrams and photographs, and there are 750 references. The book will be invaluable to all those interested in the manufacturing processes of uranium and its compounds.

D. E. R. Hughes

GENERAL ASTROPHYSICS

Astrophysique Générale

Par J. C. Pecker et Prof. E. Schatzman. Pp. x+756. (Paris: Masson et Cie., 1959.) Broché, 12,000 francs; cartonné toile, 13,000 francs.

ASTROPHYSICS is not a big subject in relation to some other sciences, but in my view the day has passed when any complete and satisfactory account of it can be compressed into one text-book, unless at a quite elementary level. Here two well-known French astrophysicists have attempted heroically to do the well-nigh impossible, and even if the result falls short of perfection it deserves a warm welcome, for good general text-books in this field are very scarce. We have on one hand a fair number of specialist monographs, some of them invaluable, and on the other more than enough glossy semi-popular and popular books, most of which should be avoided as the plague by any serious student. Between these extremes there is remarkably little.

The first 100 pages of "Astrophysique Générale" are given over to a summary of "what every young astrophysicist should know"—everything from hydrodynamics to Hamiltonians, statistics to spectroscopy. It illustrates the wide range of technical knowledge a theoretical astrophysicist ideally should command, but is much too compressed to be anything but a refresher course for a recent honours graduate in mathematics or physics. A whole book written along these lines would be very useful, but I question the wisdom of attempting the task in less than, say, 1,000 pages. Part 2, dealing with astronomical instruments and methods of observation, is at a very different level of sophistication. It shows signs of having been written by theorists, for there are a number of over-simplified or over-optimistic statements (for example, "Pour les étoiles jaunes et rouges, la mesure des magnitudes radiométrique permet d'obtenu aisément les magnitudes bolométriques"), as well as a few small errors. In Part 3, the longest in the book, the authors are, however, more on their own ground, discussing what we know of stars, their spectra, masses, intrinsic luminosities, radii, and the theories of their atmospheres and their interiors.

Part 4 deals with systems of stars, the structure of the Milky Way and of external galaxies. It also has chapters on stellar dynamics, interstellar matter and stellar evolution. Part 5 summarizes our knowledge of the Sun, which is regarded as a typical *G2V* star, and of the planets and other bodies in the solar system.

This is not a book for a beginner. The reader needs a solid background of mathematical physics and at least some prior acquaintance with elementary astronomy. There is a real need for astrophysical text-books at this level; but this one, it seems to me, attempts to do too much in too little space and one result is that in places it tends to be scrappy. I suspect that quite competent students, especially perhaps the more conscientious and thoughtful, might sometimes find its pace slightly bewildering. The production is on the whole good. Too small a type for comfort has sometimes been used in subscripts, etc. The illustrations are in general good, but a few are misleading. A certain number of misprints need correction.

R. O. Redman

PROGRESS IN THE FLORA OF CANADA

Flora of Alberta

A Manual of Flowering Plants, Conifers, Ferns and Fern Allies found growing without Cultivation in the Province of Alberta, Canada. By Prof. E. H. Moss. Pp. v+546. (Toronto: University of Toronto Press; London: Oxford University Press, 1959.) 80*s*. net.

DESPITE some 250 institutional herbaria, and some 25 journals which regularly publish taxonomic papers, in temperate North America, our broad knowledge of the flora of that continent is surprisingly fragmentary. There are large areas of the continent and large numbers of taxa which, by modern standards, have not been critically, or even adequately, examined. This should not be taken to imply that large numbers of 'new' species remain to be found in North America—for the country has generally been well explored, even if not yet thoroughly collected. Rather, it indicates the large amount of work that is yet to be done before we have even a bare catalogue which will show the extent of the North American flora.

Until very recently, the flora of Canada has been particularly poorly understood. The most south-easterly part of Canada has been treated in the two standard Floras of the north-eastern United States. Southern parts of the prairie provinces were included in the now somewhat outdated Floras of the prairies and plains, and of the Rocky Mountains of the United States. Southern British Columbia has a Flora published as long ago as 1915 (with a Supplement published in 1947). In the past twenty years, however, the botanists of the National Museum of Canada have made a concerted attack on the flora, with the view, eventually, of a proper "Flora of Canada".

The regional Floras of the National Museum of Canada, combined with Hulten's monumental "Flora of Alaska and the Yukon" (1941–50), Polunin's "Circum Polar Arctic Flora" (1959), and the various more generalized publications of the Canadian Department of Agriculture are now beginning to give us a rather good idea of the outlines of the Canadian flora. The most serious gap in our knowledge, of recent years, has been the lack of a Flora for the western prairies and the Rocky Mountains. The publication, by the University of Toronto Press, of the "Flora of Alberta", written by the distinguished Canadian botanist, Prof. E. H. Moss, is, then, an event of some considerable interest and importance.

The Province of Alberta is one of the twelve administrative divisions of the Dominion of Canada. It extends (with irregularities in the south-western corner) from the 110th degree of west longitude to the 120th degree, and from the United States boundary at 49 degrees of north latitude northwards to 60 degrees. It has an area of about 255,285 square miles. The flora, as herein enumerated, consists of some 1,605 species of vascular plants. These are the bare facts of the matter.

After some 200 years of experiment and practice, it is fairly clear to botanists what the essential qualities of a good Flora are. A Flora (as distinguished from *the* flora) is, first and foremost, a tool for the identification of any plant included within its circumscription of areal and systematic range. Basically, the most important part of the treatment is the delimitation and description of the individual taxa. These circumscriptions should be clear, precise, and as brief as possible. Supplemental data, such as descriptions of habitat, flower colour, and season of flowering are frequently of considerable practical usefulness.

For the general user, however, the most important parts of a Flora are the 'keys'—analytical tables of pairs of contrasting characters, set out in a conventionalized form, by which one should be able to be led, through the sets of alternatives, to the name and description for the taxon of which the user has a representative in hand. Indeed, many very useful Floras consist, essentially, of keys alone. To be useful, a key must be infallible. Infallible is a strong word—but if the taxonomy of the text is an accurate reflexion of the facts (plants) found in Nature, infallibility is practically possible. The large number of practically infallible keys in Floras and monographs which are in general use is sufficient proof of this statement. Keys which do not work very frequently indicate taxa which are not adequately understood.

The "Flora of Alberta" is an extremely valuable tool, which should have considerable usefulness both in the herbarium and in the field. It is obviously based on the author's first-hand knowledge of the Province. The descriptions are generally clear and concise. The keys to the families and to the genera seem to be rather good examples of their kind. The keys to the species are occasionally a little less happy, especially when qualitative, rather than quantitative, characters are relied on too heavily (*Salix* and *Senecio* afford examples of this).

The "Flora of Alberta" is, as the author comments in his preface, "a pioneer effort". As a pioneer effort we are grateful that the work has been done. It is no adverse reflexion on the work of the author if we suggest ways that future editions might be improved. I think that we would like to see a few pages devoted to a discussion of the vegetation, the geography, and the geology of the Province. A map of the area would be helpful. Illustrations of some of the more interesting taxa would be useful. A short discussion of the history of botanical exploration in the Province would also be of interest, and would add a welcome perspec-

tive. Notes of flower colour and season of flowering would enhance the usefulness of the Flora to the layman.

It is very easy for those of us who have been brought up in regions that are well known botanically to pick flaws in a pioneer work covering an area that is little known. We should remember, when we are tempted to criticize, the very great debt we owe to men like Prof. Moss (need we mention Ridley, Asa Gray, or J. D. Hooker), who, in their retirement, have not been content to rest, but have, instead, given us basic works to build on. Their errors may or may not be glaring. They, not we, have done the work.

GORDON P. DEWOLF, JUN.

THE CHEMISTRY OF AIR POLLUTION

The Chemical Analysis of Air Pollutants

By Dr. Morris B. Jacobs. (Chemical Analysis: a Series of Monographs on Analytical Chemistry and Its Applications, Vol. 10.) Pp. xviii+430. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 102*s*.

ONE need not be a chemist to appreciate the ever-growing menace of air pollution in urban communities. Too often the discomforts and dangers of the winter 'smog' descend on a choking populace, apparently powerless to alleviate the distress caused by its own machinations. This is pollution at its obvious worst, but there are many other forms of pollution which though less conspicuous are no less hazardous and indeed, in the case of radioactive contamination, can have such far-reaching effects that the entire populace of an affected area must be evacuated.

In order to control air pollution, it is first necessary to measure it, and this involves the determination of the nature and amount of the contaminating materials. In this book, Dr. Jacobs, who is a well-known consultant in this field, sets out his systematic approach to the many chemical and physical problems involved in analysis of gaseous and particulate contaminants in air.

Chapter 1 contains a general account of sampling and the available means of taking samples for analysis. Chapter 2 is devoted to the measurement of volume, quantity, and velocity of gases. Chapter 3 considers sootfall and dustfall, and the analysis of soots and dusts by a number of standard methods. Chapter 4 deals with the evaluation of atmospheric dust, particularly the particle sizes involved. Chapter 5, on suspended particulate matter, gives procedures for the chemical analysis of organic and inorganic constituents. Chapters 6 and 7 deal respectively with smoke density and smoke shade, and the sampling and analysis of industrial stack-smoke. Chapters 8 and 9 cover the chemical analysis of sulphur and halogen-containing air pollutants, Chapter 10, that of nitrogenous compounds and ozone, Chapter 11, oxides of carbon, cyanide, and phosgene, and Chapter 12, general organic compounds. In Chapter 12 these materials are arranged according to their functional groupings. Chapter 13 covers the determination of radioactivity and the detection and determination of hazardous isotopes such as strontium-90. The analysis of incinerator-flue gases and motor-vehicle exhaust gases is dealt with in Chapters 14 and 15. Chapter 16 deals with the interesting subject of 'odour' analysis, which involves the determination of the amount of a (generally) malodorous material in the atmosphere. The final chapter (18) describes instruments used to monitor particular types of air contaminants. An appendix contains a number of useful tables and data pertinent to the information given in the text.

The wealth of information given in this book and the concise and systematic way in which it is presented must make it an obvious choice for all who are interested in the control of air pollution. Its use is not restricted in any way by its contents which are directed primarily to the analyst, but are of interest to a much wider section of the community, such as engineers, factory inspectors, public health and sanitation officers. Much of the analytical chemistry can be adapted for courses in colleges and universities, and the inclusion of many simple and inexpensive methods is of great value not only to teaching institutes, but also to the many communities and industrial organizations which do not have the funds necessary to set up the more elaborate methods and instrumental techniques.

For the analytical chemist, this book provides an admirable addition to the literature on applied analysis. It maintains the high standard of its predecessors in the Interscience series of Monographs on Analytical Chemistry and its Applications, and it must undoubtedly become a standard work on the subject of air pollution.

W. I. STEPHEN

VEGETABLE PATHOLOGY

Vegetable Diseases and Their Control

By Prof. Charles Chupp and Prof. Arden F. Sherf. Pp. v+693. (New York: The Ronald Press Company, 1960.) 12 dollars.

ALTHOUGH directed primarily at the American reader this publication should prove of interest to those in Great Britain and elsewhere.

After preliminary sections on seedling diseases and those affecting a range of host plants, there are sixteen chapters each dealing with the diseases of a group of vegetables. Potatoes are not included. The book concludes with chapters on minor element deficiencies, nematodes and soil sterilization. A valuable feature is the mention of varieties that show resistance to the various diseases.

As indicated in the preface to the volume, an attempt has been made to write in as nearly a non-technical manner as possible so that the book may be of use to the amateur as well as to the commercial grower. Considerable success has been achieved in this respect and the narrative style is very readable, a feature which is assisted by the excellent clear type. The sections abound in practical recommendations for control and obviously contain the fruits of many years experience in this field.

The book is also intended to serve as a text for students, research specialists and advisers, but its value in this respect is less apparent. There are few sub-headings within the sections on each disease; with a few minor exceptions there are no drawings or photographs of the causal organisms, and little or no mention is made in the text of the references quoted at the end of each section. These therefore

lose much of their value and they may also be criticized on the grounds of incompleteness. The work and monograph of Colhoun on clubroot of crucifers, for example, receive no mention, and the chapter on soil sterilization is accorded five very meagre references (this has since been found to be due to the printers omitting in some copies a page of references).

Some of the control measures now seem rather old-fashioned (for example, soaking seeds in copper sulphate solution to control certain damping-off diseases). Errors also occur in several places. The photograph of the effect of *Verticillium* wilt on tomato leaves is not of the normal symptoms associated with the disease; Bordeaux mixture is not used (as stated) against *Didymella* stem-rot of tomatoes; the section on big vein of lettuce does not give an accurate representation of the latest information or experiments on the disease.

The publication gives the impression that in attempting to cover a very wide range of subjects and of readers the authors have only partially succeeded. Even so, the book does provide a useful compendium which may with advantage be used both as a guide to some of the other sources of information on the subject and as a supplement to them.

W. G. KEYWORTH

KNOWING OURSELVES

Understanding Human Society

By Prof. Walter Goldschmidt. (International Library of Sociology and Social Reconstruction.) Pp. 253. (London: Routledge and Kegan Paul, Ltd., 1959.) 21*s*. net.

THE distinguished editor of the *American Anthropologist*, Walter Goldschmidt, has essayed a most difficult task—to provide a guide to the development of man in society. Such a book has long been needed. The great majority of anthropologists have for too long been too preoccupied with the immediate problems of their subject. There can be little doubt that studies of kinship have dominated the anthropological horizon for a considerable time. It is refreshing, therefore, to come upon a book which attempts to deal with the broader implications of the subject.

One of the most valuable sections of this book is entitled "The Dimensions of Anthropological Theory". It begins, "The ultimate task of the anthropological enterprise is to explain the uniformities and diversities in the natural condition of mankind . . .", and proceeds to a discussion of the various approaches which have been made to the study of man. Curiously enough, the history of anthropology, with the exception of Haddon and Penniman, is extraordinarily sparse. For the student this chapter fills a long-felt want. The teacher is apt to presume a knowledge on the part of the student which does not always exist. Frequently he is too concerned with his own bias to worry about the theories of others. The individual who sat at the feet of the late Father Schmidt in Vienna would scarcely have obtained an unbiased account of, say, Malinowskian functionalism. Prof. Goldschmidt, on the other hand, is remarkably fair in his treatment of the theories of others.

In developing his theory of social evolution, which forms the core of the book, the author is at pains to point out that we must exclude any idea of moral values which so bedevilled the old evolutionary hypotheses. The theory presented is eminently respectable, and few would quarrel with it. Its fault lies in the fact that it does not take us very much further on the way. "It does not in and of itself explain these social systems, in the sense that it offers a full account of what makes them as they are." Perhaps no theory could; but we are back where we started being forced to consider each society as a unique whole.

The value of this book is perhaps not in the field of original theory but rather in the clarity and succinctness with which the author deals with the ideas of others about the nature of human society. In the jargon-ridden jungle of the social sciences, Prof. Goldschmidt has created a little oasis of simplicity for which we must be grateful. It must be admitted that Americans are not usually exemplars in this matter.

The publishers have not been too well served by the printers who, by using a different type for the concluding words or sentences of chapters, have managed to convey an arcane sense which is totally misleading.

F. HENRIQUES

SOCIOLOGY OF CASTE IN CENTRAL INDIA

Caste and Kinship in Central India

A Village and its Region. By Adrian C. Mayer. (International Library of Sociology and Social Reconstruction.) Pp. xvi+295+16 plates. (London: Routledge and Kegan Paul, Ltd., 1960.) 35*s*. net.

THIS is a sociological study of caste as it operates in Central India in the E. M. Forster country, and it provides a valuable addition to the literature on caste in India. Much has been written on this subject, but mainly on a broad and generalizing and on an India-wide scale, or in a theoretical, evolutionary or historic form. What are lacking are the detailed studies of caste as it actually functions in specific Indian communities, against which these generalizations and hypotheses can be tested. Dr. Mayer's book is one of the best studies of this sort that has yet been made and the only one that deals with the caste system as it operates in a multicaste village and its surrounding neighbourhood. It brings out very clearly the interconnexion between kinship, sub-caste and caste. Village boundaries are shown to be something more than territorial and to mark the difference between two kinds of relationship, that of common caste and of agnatic kinship (in the village) and that of common sub-caste and of bilateral and affinal kinship (in the region).

The book is divided into three parts: the first sketches the historic and economic background, the second examines intercaste relations as they affect ritual, economic and political status and the third analyses the constitution of the caste, its internal structure, the part played by unilinear descent, and the pattern of marriage and of social control within the sub-caste.

Social anthropologists interested in kinship, whether or not they are also concerned with the study of caste, will find much of value in this study, while those more immediately concerned with rural Indian political and economic development would do well to read the chapters on caste and village leadership and on the economic aspects of caste.

G. I. JONES

Advances in Applied Mechanics

Vol. 6. Edited by H. L. Dryden, Th. von Kármán, and G. Kuerti. Pp. x+294. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 9 dollars.

THIS latest volume of the series is concerned entirely with fluid mechanics. There are two chapters on boundary layers: one on unsteady layers, by K. Stewartson; the other on layers in a dissociated and ionized gas, by G. Ludwig and M. Heil. The two following chapters are on high-speed flow: the first on shock propagation along varying ducts, by W. Chester; the second, a particularly valuable account of similarity and equivalence, by K. Oswatitsch. The last chapter, a short one by R. Wille, is on Kármán vortex streets.

Reading through this latest collection of essays on topics in applied mechanics, one is made to realize once again what a remarkably sound idea the publication of this series of volumes has been. To the expert who has already formed his own balanced view of a subject, an individual essay may not always seem worth while; partly because, no doubt, he disagrees with the view taken by the author, and partly because there is not usually much original material to compensate for other shortcomings. But to the newcomer, whether he be a complete novice or a more experienced person broadening his interests, the publication of a detailed and up-to-date account of a subject, representing the personal view of someone who has usually taken an active part in developing it, is a valuable service—much more valuable than the publication of the few summarizing paragraphs, followed by several hundred references, that sometimes pass for a review. The editors, no less than the latest additions to the list of authors, are to be congratulated for maintaining this service.

IAN PROUDMAN

Viscoelasticity

Phenomenological Aspects. Edited by J. T. Bergen. (Symposium sponsored by the Armstrong Cork Co., held at its Research and Development Center, Lancaster, Pennsylvania.) Pp. x+150. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 6 dollars.

SOME explanation is required concerning the definition of terms in the title of this book. "Phenomenological aspects" are clearly defined as those concerned with the material "as a continuum which is characterized by specific, fundamental parameters"; as opposed to aspects "dealing with molecular structural or molecular model considerations". Viscoelasticity is taken to include behaviour involving flow, more often currently described as elastico-viscous. Both linear and non-linear relations are discussed but there is some confusion over the definition of "linear". One contributor gives alternative definitions implied to be synonymous (p. 28), although it is quite possible to find materials (for example, those obeying Bach's equation) the behaviour of which would be linear according to one version of the definition but non-linear following the other.

With some exceptions, the equations developed in these essays are applied by the authors to large masses of data from work published elsewhere, usually on materials which can be tested over wide ranges of stress and many decades of time. Only a few types of test are feasible under such conditions and it is remarkable that sufficient superposability exists to make possible so good a measure of agreement as has been found.

The book is important in correcting a tendency, prevalent in certain quarters, to believe that the only meaningful approach to rheology is through molecular considerations. It is a pity that one or two of the essays are written in such bad English, as judged by either British or American criteria, as to be irritating to the reader.

G. W. SCOTT BLAIR

Organic Chemistry

By Dr. I. L. Finar. Vol. 2: Stereochemistry and the Chemistry of Natural Products. Second edition. Pp. xi+834. (London: Longmans, Green and Co., Ltd., 1959.) 45*s*. net.

THE second edition of Vol. 2 of Finar's "Organic Chemistry" matches the high class of the third edition of Vol. 1. These new editions were both published in 1959. They are designed to provide a foundation for the organic syllabus of a special honours degree course in chemistry; this objective has been achieved. Present authors of text-books suitable for this level have to concern themselves with deciding what can be left out, and Finar's selection has obviously been made carefully. He has included practically all those topics of fundamental importance, but some quite recent developments are also introduced in such a way that the interest of the reader is excited. A valuable feature is the comprehensive list of reviews and monographs given with each chapter.

The discussion of stereochemistry occupies 210 pages. It is clear and covers optical and geometrical isomerism, the stereochemistry of the diphenyls and the stereochemistry of elements other than carbon. This is balanced by an introduction to more recent developments such as the stereoelectronic features of chemical change and conformational analysis.

The major part of the book is devoted to the determination of the structure and the synthesis of the more important classes of natural products. These have been carefully selected and include carbohydrates, steroids, amino-acids, proteins, alkaloids, anthocyanins, nucleic acids, porphyrins, vitamins and antibiotics. This is the best treatment of these topics which is easily available to undergraduates. There are certain gaps in the coverage provided by Vols. 1 and 2 of this work, but this is inevitable. The books are easily read, and this is a pleasant change from those which are just catalogues of structures and reactions. The second edition of Vol. 2 is a better book than the first edition and can be warmly recommended.

W. D. OLLIS

Scientific Manpower

By Joyce Alexander. Pp. viii+135. (London: Hilger and Watts, Ltd., 1959.) 15*s*. net.

WHAT factors determine whether a young person does or does not become a scientist? This is the question which Mrs. Alexander examines in this carefully documented essay. She points to the shortage of scientific man-power; she examines the educational system which has failed to overcome the shortage; and she discusses the proposals which have been made to overhaul the educational system and to equip it to serve contemporary needs. There is a very sensible chapter on scientific woman-power. This is a neat and useful little book. It does not break fresh ground, but it equips the reader to do some thinking for himself.

RECENT RE-ENTRY RESEARCH AND THE COSMIC ORIGIN OF TEKTITES

By DEAN R. CHAPMAN

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OPPOSING views have been expressed in recent years as to whether tektites are terrestrial or cosmic in origin[1–5]. The purpose of this article is to outline some new results obtained by bringing to bear on the problem recent advances from the discipline of re-entry aerodynamics. It is concluded that the australite tektites show sufficiently clear and diverse indications of atmospheric entry to enable their approximate initial velocity and flight path angle to be determined. A surprisingly narrow band of entry velocity is delineated which is in the cosmic-origin range, and, more intriguing, in that particular range uniquely compatible with origin from the Moon.

Although the present work is restricted to australite tektites, this does not limit the generality of the end result. The various tektite groups unmistakably are related by a family-like chemical composition and internal structure; hence, the determination of cosmic versus terrestrial origin for one group also applies to the other tektite groups within the family.

Australite Entry Aerodynamics

It has long been known that australites have been twice melted, and that the second melting occurred superficially on the front surface only. From this and other evidence, Baker[1] has concluded that the australites entered the atmosphere as cold, independent bodies, most of which neither tumbled nor rotated during ablation. Recent re-entry research provides three additional lines of evidence crystallizing this conclusion. During an experimental study in 1959, D. R. Chapman and H. K. Larson (at the Ames Research Center) found that the ablation of glass bodies commonly proceeds through the formation of ring waves being propagated radially away from the stagnation point; strikingly similar waves of 'flow ridges' are exhibited on many australites[1] and on a few javites[5]. A second line of evidence concerns the displacement of a glass particle within an ablation layer. Within the thin, receding, melted layer, the particle displacement near a stagnation point varies essentially exponentially with depth below the surface, and essentially linearly with radial distance from the stagnation point[6]; these same two types of mathematical variation were found in photographic enlargements of the australite thin section B in plate X of Baker's monograph[1]. The third line of evidence arises from a study of australite shapes. At least 98 per cent represent stable aerodynamic configurations in hypersonic flight when orientated in the unique manner that is compatible with the orientation demanded by the directions along which the secondary melt has flowed on their surfaces. Without going into the aerodynamic details, it is noted that such general aerodynamic stability is to be expected only in descent through the atmosphere, and not in ascent[7]. The overall evidence leaves no doubt that aerodynamic heating during entry into the atmosphere has been responsible for the second period of australite melting.

Even an absolute proof that an object has entered the atmosphere and suffered ablation at hypersonic velocity does not prove that it is cosmic in origin. The particular numerical value of the hypersonic velocity is of crucial importance. All that has been said about australite entry aerodynamics would apply, for example, equally well for 6 km./sec. entry velocity as for 12 km./sec. Yet, entry at 6 km./sec. could only be from a terrestrial source, whereas 12 km./sec. could only be from a cosmic source (since the Earth escape velocity of 11·2 km./sec. lies in between). Consequently, the aerodynamic evidence for tektite origin hinges on the magnitude of the velocity.

Only through relatively recent developments in re-entry research has it been possible to determine the entry velocity of the australites. Knowledge was required of the rate of aerodynamic heating as developed recently through both theory[8] and experiment[9], and of the rate of ablation of silica-rich glass as given by a refined version of the Bethe-Adams theory[6] recently confirmed in the laboratory[10]. In computing trajectories extensive use was made of Z-function solutions[11] for shallow supercircular entry. Through the use of high-speed digital computing machines the required Z-functions were compiled[12].

The analysis also required knowledge of certain physical characteristics of tektite glass, the most important of which is the viscosity-temperature relationship as determined from experiment[13]. Detailed data on the mass, dimensions, and radii of curvature of complete, well-preserved specimens were obtained from Baker's research[1], from additional correspondence with him, and through personal measurement of australites in the British Museum.

Entry Conditions and Geographical Distribution

The limited geographical distribution of a fall provides useful restrictions on the entry velocity. Let us consider first the hypothesis of terrestrial origin, wherein tektites are assumed to result from some violent natural phenomenon which has fused Earth material and thrown the melt far above the atmosphere (far enough to have had time to solidify before re-entering and experiencing the second melting). The exit velocity from the atmosphere would equal the entry velocity; it could not exceed some maximum value and still confine the fall to a limited geographical area. Velocities as high as the orbital velocity of 7·9 km./sec., for example, would spread the fused earth around the globe, and hence are too high to be compatible with a terrestrial origin hypothesis. If the fused earth were hurled in the manner that ejectamenta from hypervelocity impact in stone are hurled[14], then the maximum entry

velocity consistent with a terrestrial origin and confined distribution would be about 6 km./sec. According to the hypothesis of cosmic origin, however, the entry velocity would have to be equal to or greater than 11 km./sec. for direct entry (indirect entry after multiple-pass atmosphere braking[13] is not considered, as it would have resulted in global distribution of a cluster). For cosmic origin, all individual specimens in a tektite cluster would have the same entry velocity.

Results of Analysis

The approximate entry velocity has been determined from: (1) the thickness of the ablation layer near the stagnation point, as given by the displacement of internal glass striæ; (2) the amount of ablation at the stagnation point, as given by the shapes of complete, well-preserved specimens. For each entry angle γ_i (measured relative to local horizontal) the particular entry velocity V_i was calculated which would be compatible with the observed characteristics of a given australite. Entry angles were considered within the range from 90° (vertical entry) down to the overshoot boundary (nearly horizontal entry in which barely enough drag is encountered to land the tektite). In this way a V_i (γ_i) curve is obtained, some point along which the true V_i and γ_i would be located. By computing several independent curves a limited domain of entry conditions is delineated.

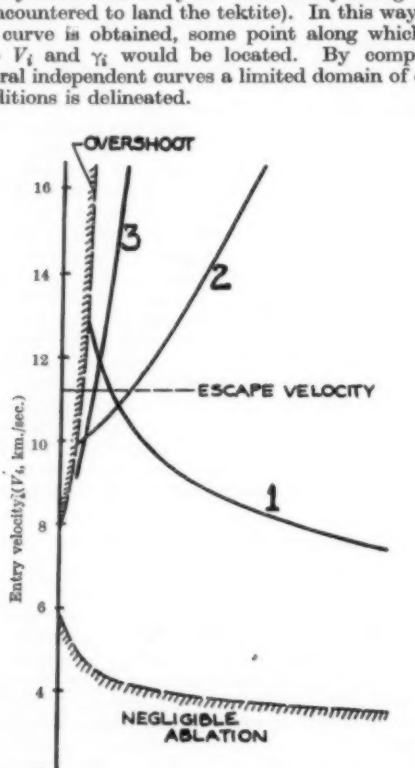

Fig. 1

The essential results are illustrated by curves in Fig. 1. Curve 1 corresponds to the entry velocity computed from the displacement of glass striæ in thin section *B* of plate *X* of Baker's monograph. Curve 2 corresponds to the velocity computed from the amount of ablation of "perfect button 1212" in Baker's collection. This particular button possesses a complete flange large enough to account for nearly all of the mass melted during entry. It is representative of those buttons which have lost the least amount of mass during entry. Curve 3 corresponds to the same type of calculation as curve 2 only for a large core (Reg. No. 1926–349 in British Museum). This curve is representative of an average large core. Some cores show less ablation and would fall between curves 2 and 3—where most buttons also would fall—while other cores show more ablation and would fall a short distance to the left and above curve 3. All three curves represent specimens found locally in a relatively small area of Victoria. In order for these australites to have entered with essentially a common velocity, this velocity would have to be in the range between about 10 and 13 km./sec.

By invoking certain dynamical limitations, the range of australite entry velocity is narrowed to considerably less than the 10–13 km./sec. band. At the lower end, entry in the 10–11·2 km./sec. range would correspond to terrestrial origin; at the entry angles indicated such velocities would have resulted in world-wide tektite distribution, and hence are rejected. At the upper end, velocities much above 11·2 km./sec. also are rejected, although for entirely different reasons. At 12 km./sec., for example, the required difference in entry angle of between 6° and 17° would correspond—for two specimens falling on the same spot—to impact about an hour apart. Since the approach velocity far from the Earth is 4·4 km./sec. for $V_i = 12$ km./sec., a time-interval of 1 hr. between impacts in Victoria would correspond to a distance interval when far from the Earth of greater than the Earth diameter. It is unreasonable to expect a cluster of such dimensions to land on a confined area of Australia. At entry velocities only slightly greater than the escape velocity (say, V_i of about 11·3 km./sec.) the approach velocity far from the Earth is small, so that the cluster dimensions implied by the indicated differences in entry angle also are small, and thus compatible with the limited area of the australite strewnfield. After imposing such limitations, the only entry velocity range we are left with is the narrow interval a fraction of a km./sec. above the escape velocity. This velocity band is compatible with a lunar origin of the australites. In fact, the Moon is the only known celestial body for which the entry velocity would be expected to be in this particular narrow range.

A note is in order here about the accuracy of the calculations. All equations employed are based on analytical methods that have been verified in the laboratory. However, several physical approximations were employed for simplicity in the computations. For example, in making trajectory calculations the variable mass was approximated by the average before and after entry (specimens were selected which have lost only a small or moderate amount of mass during entry in order to minimize this uncertainty). The estimated accuracy is less than about 2 km./sec. in velocity. Shifts in the various curves of an amount corresponding to the estimated accuracy would not affect the end-result that the

observed features of australites are compatible with a cosmic entry velocity of essentially the Earth escape velocity, and incompatible with the hypothesis of a terrestrial origin.

Among approximately thirty serious hypotheses known to me which have been advanced during the past century in an effort to explain the perplexing origin of tektites, the Moon has had a fair share of supporters, just as have the stars, the Sun, Earth lightning, volcanoes, comets, lost planets, lost Earth satellites, and unknown prehistoric races remarkably advanced in glass technology. In view of this, it seems appropriate to mention the early advocates of a lunar origin. In 1897 Verbeek[15] suggested that volcanic eruptions on the Moon were a possible source of tektites. An alternative mechanism was suggested in 1940 by Nininger[16], who regarded meteorite impact on the Moon as a probable mechanism for dislodging lunar rock with sufficient velocity to escape the Moon and land on Earth.

Neither lunar volcanic activity nor meteoritic impact on the Moon can be ruled out to-day as being unrelated to tektites. For decades the Moon has been generally regarded as a dead celestial body without remnants of any volcanic activity it may have had in the past. This view has been drastically shaken recently by Kozyrev[17], who obtained spectroscopic evidence of gas escaping from Alphonsus crater in 1958, and of a 1200–1500° K. surface temperature temporarily existing in the same crater in 1959. Inasmuch as lava can bring up material which is lighter and also richer in radioactive elements than the average lunar composition, this provides a simple explanation of why the density of tektites (2·3–2·5) is significantly lower than the Moon's average (3·3), and also why tektites, just like Earth eruptive rocks, are relatively more rich in uranium and thorium than are meteorites. Thus, lunar volcanism may enter the tektite picture, at least indirectly. At the same time, the recent experiments of Charters and Summers on hypervelocity impact in stone[14] have indicated a ratio of backsplash velocity to impact velocity (about 0·3) which leaves no doubt that it is possible for meteorites coming from the asteroidal belt to eject debris beyond the Moon's gravitational field. Present knowledge is too primitive to warrant complacency as to how lunar material may have arrived on Earth.

In summary, the new results from the discipline of re-entry aerodynamics assign a cosmic origin to tektites, and point firmly at the Moon as somehow being involved in the act of hurling tektites to the Earth.

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MEASUREMENTS OF CÆSIUM-137 IN HUMAN BEINGS DURING 1958-59

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EVER since the first reports in 1956[1] that cæsium-137, a fission product from nuclear bomb explosions, was present in human beings, there has been considerable interest in estimating the contribution which this material makes to man's radiation dose. In view of this we have, since January 1958, attempted to measure the amount of cæsium-137 in all persons who have been referred to us for a measurement of their body radioactivity. By far the largest group of these people were women who had worked in the radium-luminizing industry and had ceased working at the end of the Second World War. There is no reason for suspecting therefore that any of them had been in contact with cæsium-137 other than that from nuclear bomb fall-out. They came from a wide area around London, the majority living within 50 miles of the City, although some came from so far afield as Leicester, Swansea and Folkestone. We are now reporting the results of our measurements up to the end of 1959 on 203 of these luminizers, 182 females and 21 males. Besides measuring their radium and cæsium contents we have also estimated their body potassium from a measurement of its naturally occurring isotope, potassium-40. In addition, we have estimated the mean dose of radiation received by these people as a result of the cæsium-137 in their bodies. For comparison, we are including the results of cæsium-137 measurements and calculations of dose for the same period on 16 members of the staff of the Radiological Protection Service.

The amounts of all three materials were estimated by measuring their gamma-ray activities. This was

done in a low-background laboratory using, as the detector, four sodium iodide (thallium activated) crystals situated above the surface of the body. The crystals were optically coupled to photomultiplier tubes, the outputs of which were amplified and fed to a 100-channel pulse-height analyser.

All persons were measured for a period of 1 hr., preceded or followed by a measurement of the background with a water-filled inert model of the human body weighing 70 kgm. in place of the subject. The amounts of the radioactive materials in the people were then determined by comparing the gamma-ray spectrum from each subject with that from calibration sources. It was assumed, in accordance with the views of the International Commission on Radiological Protection[3], that cæsium-137 and potassium would be uniformly distributed throughout the whole body and that radium would be uniformly distributed in the skeleton only. For cæsium-137 or potassium, the calibration sources were polythene models of the human body filled with solutions either of cæsium-137 chloride or of potassium chloride of known concentration. We have found that the calibration so obtained varied very little with the size of the model. Calibration for radium consisted of determining the response to a point source of radium at several positions along the central axis of the model used for the background measurements. The positions used corresponded to the anatomical regions, head, thorax, pelvis, thighs, legs and arms. In order to obtain a calibration which would approximate to that from a uniform distribution of radium in the skeleton, the contribution from the source at each position was weighted according to the mass of the skeleton in each of the six regions.

Cæsium-137 and potassium-40 emit single gamma-rays of 0·66 MeV. and 1·46 MeV. respectively, and the scintillations which they generate in the crystals following photo-electric absorption produce peaks in the counting-rate spectrum obtained from the 100-channel analyser. The body burdens of cæsium-137 and potassium-40 were determined from the counting-rate in their respective photo-peaks. However, some photons from potassium-40 lose energy due to scattering in the body and in the apparatus, and then contribute to the counting-rate in the cæsium-137 photo-peak. An appropriate allowance must be made for this when estimating cæsium-137. An additional uncertainty arises when the subject also contains radium, since this element, together with its radioactive daughters, emits a series of gamma-rays with energies ranging from 0·2 MeV. to 2·4 MeV., and so contributes to the counting-rate in both the cæsium-137 and potassium-40 photo-peaks. The radium burden of the subject may be determined unambiguously from the counting-rate corresponding to photons having energies greater than that from potassium-40 ; in practice, an energy-band from 1·7 MeV. to 2·6 MeV. was used. It is clear, however, that where radium poisoning is suspected, even if the radium burden appears to be zero, an additional uncertainty is introduced into the measurement of cæsium-137 and potassium-40 by the error of the radium measurement. For this reason, the standard error of estimating potassium due to counting errors alone increases from 8 gm. where radium can be ignored to 13 gm. for a luminizer, and that of cæsium-137 from 1 mμc. to 2 mμc. These additional errors vary only slightly with the radium content. As the radium burden increases, however, the identification of the cæsium-137 and potassium-40 photo-peaks becomes increasingly difficult, and it was necessary to limit the cases selected to those having small radium burdens. The 203 luminizers selected all contained less than 0·02 μc. radium-B in equilibrium with radium-C, the principal gamma-emitting daughters of radium ; these were about 85 per cent of the luminizers referred to us.

The principal interest in these measurements is in estimating the radiation dose from cæsium-137, and this depends on its concentration in different parts of the body. It has been suggested by Langham and Anderson[2] that since cæsium is chemically similar to potassium they might also behave the same metabolically. These authors and others[4] have therefore expressed the concentration of cæsium-137 in the body in terms of a cæsium-137/potassium ratio. From a mean value of this ratio for a group of individuals, they have calculated the mean radiation dose to the group, assuming that the average man contains about 140 gm. potassium and that the cæsium-137 is uniformly distributed throughout his body of weight 70 kgm. However, if the isotope is distributed uniformly throughout all body tissues, it is important to know the way in which cæsium-137 varies with the weight of the individual. We have therefore analysed the way in which cæsium-137 varies with body-weight and potassium in the largest group of our series of measurements, namely, the 182 female luminizers. Their average age was 41·6 yr. with a standard deviation of 8·5 yr. The youngest member of the group was 27 and the oldest 75.

In order to test any possible trend of the body-burden of cæsium-137 with time, the results for eight quarters during the period January 1958–December 1959 were analysed separately. For each quarter it was possible to fit a multiple linear regression of cæsium-137 on potassium and body-weight. This fit was compared with the linear regression of cæsium-137 on either weight alone (ignoring potassium) or on potassium alone (ignoring weight). It was found that there was a small increase of cæsium with both body-weight and body potassium. However, the correlation of cæsium-137 with potassium could be entirely accounted for by the fact that both potassium and cæsium-137 tend to increase with increasing body-weight. (The increase of potassium with increasing body-weight is well known[1]. In our group of females, the least squares fit to all 182 measured values was $K = 71 + 0{\cdot}51\ W \pm \Delta$, where K is the potassium content in gm., W is the body-weight in kgm., Δ is a random variable with zero mean and standard deviation of 15 gm. The standard error of the estimate of the slope was 0·12. Anderson[5] also finds a non-proportional increase of potassium with body-weight that is about the same as ours, but for the same body-weight the average potassium values found by him are about 15 gm. less than ours.)

In other words, an equally good fit to the data was obtained by the linear regression of cæsium-137 on weight alone. The slope of the line was actually calculated for each quarter and its variation appeared to be random. Since we would not expect it to change with time, a mean value was taken for all eight quarters. The fitted parallel lines for the separate quarters are given by :

$$Z = A + Bx \pm \varepsilon$$

where Z is the cæsium-137 content of any individual in the group in mμc. ; A is the average cæsium-137

Table 1. Average Cæsium-137 Content of an Individual of Weight 60 kgm.

		No. of people measured	A (in mμc.)
1958	1st quarter	11	5·83
	2nd "	22	6·15
	3rd "	25	5·53
	4th "	36	5·30
1959	1st quarter	31	5·67
	2nd "	22	3·59
	3rd "	10	5·45
	4th "	25	6·46

content of an individual of weight 60 kgm. and is given in Table 1 for each quarter; B is $0{\cdot}051 \pm 0{\cdot}017$ mμc./kgm.; x is (body-weight $-$ 60) in kgm. ε is a random variable with zero mean and standard; deviation of 2·24 mμc. (a large fraction of this may be attributed to the standard deviation of the counting (2 mμc.), so that the standard deviation attributable to individual variations about the mean is about 1 mμc. cæsium-137 $[\sqrt{(2{\cdot}24^2 - 2^2)}]$).

Table 1 shows that there is no obvious trend of A with time. The result for the second quarter of 1959 appears to be low. This result was not due to any change in the sensitivity of the apparatus, nor does it appear that the ages of the persons examined in this period or the localities in which they live present any unusual features. In the absence, therefore, of any explanation for the low value, a mean value of A was calculated for all eight quarters. This was found to be 5·5, so the average cæsium-137 content of an individual in the series during 1958 and 1959 is given by:

$$Z = 5{\cdot}5 + 0{\cdot}051\,x \text{ mμc.} \qquad (2)$$

or

$$Z = 2{\cdot}44 + 0{\cdot}051\,W \text{ mμc.} \qquad (3)$$

where W is the body-weight in kgm.

Although this represents only a small increase with body-weight, it is much too large to be attributed to chance. Obviously, the cæsium-137 content in different people is not proportional to their body-weight, nor to their potassium.

As yet there is no information available to indicate whether cæsium-137 is better correlated with any body parameter other than total body-weight, and we have therefore assumed that it is uniformly distributed throughout the body. Following the calculations outlined in the Recommendations of the International Commission on Radiological Protection[2], the average dose-rate to the whole body, D, for an individual of weight W kgm. and cæsium-137 content Z mμc. is given by:

$$D = 11\frac{Z}{W} \text{ m.rems/year} \qquad (4)$$

The value of D for a female luminizer during the period in question may then be derived from equation (3):

$$D = \frac{27}{W} + 0{\cdot}56 \text{ m.rems/year}$$

The lowest weight in the 182 cases was 33 kgm. and the highest 95 kgm. The corresponding dose-rates are about 1·4 m.rems/yr. and 0·8 m.rem/yr. respectively. About half this range of body-weights would include nearly two-thirds of the 182 cases. If the radioisotope is not uniformly distributed throughout the body, some body-organs will, of course, receive a greater dose.

The number of persons measured in the other three groups, the male luminizers and the male and female staff at the Radiological Protection Service, were too small to justify an analysis of the type described above. We have, however, compared their measured cæsium-137 content with those which would be predicted by equation (3) and the mean values for each group are given in Table 2. The measured cæsium-137 content of the male luminizers during 1958 and 1959, and of the female staff at the Radiological Protection Service during 1958, were not significantly different from those predicted. However, the measured values were higher than the predicted values for the male staff at the Radiological Protection Service during 1958 and for both male and female staff during 1959. The reason for these higher values is not obvious. It is possible for members of the staff at the Radiological Protection Service to have ingested or inhaled these small additional amounts of cæsium-137 while at work, but the people found to have most cæsium-137 were not those exposed to the greatest risk. (It might be noted that the staff at the Radiological Protection Service are much younger than the luminizers; mean ages 24 against 42 for the females and 25 against 50 for the males).

The radiation dose-rate for each individual was calculated from the measured cæsium-137 content using equation (4). The mean values for each group are given in the final column of Table 2. They are very similar to those obtained for the female luminizers, and again there was no obvious change with time. This was in marked contrast to the local gamma-ray dose-rate from fission products on the ground, which changed appreciably during the same period[6].

Table 2

Subjects	No. measured	Mean cæsium-137 content (mμc.)		Mean dose-rate (m.rems/yr.)
		Measured	Predicted	
		1958		
Male luminizers	6	6·8±1·2	5·8±0·3	1·2±0·2
Male R.P.S. staff	10	9·4±0·8	6·0±0·1	1·5±0·1
Female R.P.S. staff	5	5·6±0·4	5·5±0·2	1·0±0·1
		1959		
Male luminizers	15	5·8±0·8	6·1±0·1	0·8±0·1
Male R.P.S. staff	6	10·0±1·8	6·1±0·3	1·5±0·3
Female R.P.S. staff	4	7·2±0·4	5·3±0·1	1·4±0·1

In 1958 and 1959, therefore, the mean annual dose received by the adults measured, due to cæsium-137 in the body from nuclear test explosions, was less than 2 per cent of that from natural sources, which is about 100 m.rems/yr. (ref. 7). It was also small compared with, for example, the difference of about 20 m.rems/yr. between the doses received from the natural background by persons in Leeds[8] and Belmont[9].

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THE EPIDERMAL CELL AND THE METAMORPHOSIS OF INSECTS*

By Prof. V. B. WIGGLESWORTH, C.B.E., F.R.S.

THE visible form of the insect is defined by the outer skin or cuticle; which is the product of the single layer of epidermal cells lying beneath it. The form of the insect is thus determined by the growth changes and the secretory activity of the epidermal cell. My purpose is to approach the subject of metamorphosis through a consideration of the physiology of the epidermal cell.

The epidermal cell is interesting because it combines within itself so many functions, actual and potential—social functions as a member of the community of cells of which it forms a part, and individual functions where it is concerned primarily with its own affairs. The cell that is used to illustrate this theme is the ordinary epidermal cell of the abdominal wall in the blood-sucking bug *Rhodnius prolixus*. In its resting state this cell is flattened and attenuated. But if a wound is made in the integument, the dormant epidermal cells are stimulated to activity. The injured cells die, and their autolytic products diffuse out and 'activate' the surrounding cells; their cytoplasm increases and so does its ribonucleic acid content; mitochondria become swollen and more numerous. These activated cells migrate by amœboid movement to the wound, leaving a peripheral zone of sparse cells among which active mitosis follows and restores the normal cell density.

The response of the epidermal cells to lack of oxygen is quite different. They normally are furnished with oxygen by a rich supply of tracheoles. If the trachea to an area of the epidermis is cut, the epidermal cells restore the supply by sending out elongated filaments which attach themselves to the air-filled tracheoles of a neighbouring area and pull these towards them. These filaments may be 100–150μ long; they are clearly contractile structures which are re-absorbed into the cell when their task is done. By this means tracheoles may be brought in from distances up to 750μ.

The chief function of the epidermal cell is the provision for growth; that is, the secretion of a new and larger cuticle and the moulting of the old cuticle. The growth process in *Rhodnius* is initiated by the meal of blood. This distends the abdomen and sends a nervous stimulus to the brain which causes the neurosecretory cells to discharge their hormone. This activates the thoracic gland and causes it in turn to secrete the growth and moulting hormone (ecdyson).

The effects of the moulting hormone resemble those which follow injury. The cells are 'activated' within a few hours. By four days, cell division has begun, and by seven or eight days the epidermis forms a regular columnar epithelium ready to begin the deposition of the new cuticle. This is a complex process involving the secretion and subsequent expansion of the lipoprotein layer (cuticulin), and deposition of the inner layers of chitin and protein. During this most active phase, the epidermal cell has an elaborate cytological structure; it contains granules of a pterin pigment, great amounts of ribonucleic acid, abundant filamentous mitochondria, innumerable double membranes of endoplasmic reticulum, glycogen and various demonstrable enzymes.

When the new cuticle is nearing completion, the epidermal cells produce and discharge the enzymes protease and chitinase, which digest the inner layers of the old cuticle and absorb the products of digestion through the substance of the new cuticle. Then they secrete a mixture of protein and phenolic substances which impregnate the cuticle and form a film over the surface. They then secrete wax which crystallizes over the surface to form a waterproof film. Finally, when the residue of the old skin is shed, they secrete the phenoloxidase which oxidizes the phenolic substances to the quinones that tan and harden the cuticle, and the tyrosinase which forms the melanin pigment of the blackened regions.

Thus the epidermal cell is a functional cell with an amazing range of chemical and physiological activities. But at the same time it is an embryonic cell which retains a large capacity for differentiation.

During each moulting stage the ordinary epidermal cell may retain its ordinary form or it may differentiate to produce (i) a pair of œnocytes, perhaps responsible for lipoprotein synthesis; (ii) a dermal gland made up of four cells which contributes a layer of 'cement' to protect the waterproofing wax; (iii) a small sense organ or sensillum made up of four cells one of which is a primary sense cell that gives rise to an axon growing inwards and ultimately finding its way to the central nervous system.

It may be that this differentiation among the epidermal cells is controlled by gradients of some chemical inductor substance; and there is evidence for the existence of some kind of 'cytoskeleton' within the epidermal cell which determines its polarity in the general integument.

Apart from this differentiation which can be observed during post-embryonic life, the epidermis has already become differentiated during embryonic development into the pattern which forms the basis of the body-form. When the epidermal cells migrate and multiply during the repair of an injury, they carry with them the potentiality to form their specific component of the body pattern—such as black pigment spots or intersegmental membrane. At the next moult, when the new cuticle is laid down, there is found to be a corresponding displacement of the pattern.

Now the pattern of the abdomen in the adult *Rhodnius* is very different from that of the larval stages; and if injuries of this kind are inflicted in the larva, there are quite different changes produced in the pattern of the adult. These results serve to emphasize that the adult pattern is already latent within the larval cells; and that when these cells divide, the capacity to form particular elements in this adult pattern is transmitted to the daughter cells. But these properties remain latent and unrealized until metamorphosis occurs.

Metamorphosis is controlled by hormones. Throughout the larval stages the corpus allatum, a

* Substance of a Royal Society Tercentenary Lecture delivered on July 23.

small gland immediately behind the brain, secretes the so-called 'juvenile hormone' or 'neotenin'. In the presence of this hormone, the epidermal cells all lay down cuticle of larval type. Their capacity for forming adult cuticle remains latent. But if growth and moulting take place in the absence of the juvenile hormone, the latent adult characters are realized, and adult cuticle is laid down. That is what happens in the last stage of *Rhodnius* when metamorphosis occurs.

As can be proved by implantation of the corpus allatum or by the application of active extracts of the juvenile hormone to the surface of the insect, the hormone acts directly on the epidermal cell, producing localized patches of larval cuticle. Under experimental conditions, the adult *Rhodnius* can be induced to moult again ; and if the cells are exposed to the juvenile hormone they will lay down cuticle showing a partial return to larval characters—a partial reversal of metamorphosis.

Thus the epidermal cell has an extensive latent capacity for differentiation. It can differentiate to give rise to one or other of the various elements which make up the spatial pattern of the integument : hairs, pigment spots, intersegmental membrane and so forth ; and the same cell can produce this element in cuticle of larval type or of adult type.

The different elements in the pattern may perhaps be produced by differences in the concentration gradient of one or more chemical substances. That certainly seems to be true of the differentiation between larva and adult. Intermediate forms can be produced by intermediate amounts of juvenile hormone. In insects which have a pupal stage, there is evidence that the larva is produced in the presence of a large amount of juvenile hormone ; the pupal form arises when only a very small amount of juvenile hormone is present, and the adult appears in the absence of juvenile hormone.

The larva, pupa and adult are three forms in a polymorphic animal the manifestation of which is controlled by the timing and amount of juvenile hormone secretion. According to this way of looking at things, metamorphosis, polymorphism, and the differentiation of the various parts of the body are closely analogous phenomena, each of which can be described in terms of the controlled realization of genetic potentialities in the epidermal cell.

LEADERSHIP IN RURAL SOCIETIES

ON Friday, September 2, the Geographical and Anthropological Sections of the British Association for the Advancement of Science held a joint symposium at Cardiff on "Leadership in Rural Societies", under the chairmanship of Lord Rennell of Rodd. The organizers of the symposium had arranged for four opening speakers drawn from England, Scotland, Ireland and Wales, respectively, hoping in this way to obtain as complete a coverage as was possible of the general conditions in the British Isles at present. The opening speakers dealing with sample studies drawn from England and Scotland were lecturers in geography, while those who dealt with Irish and Welsh conditions were university teachers specializing in social anthropology.

Two matters were at once apparent. The four opening speakers were concerned with the rapid decline of native leadership in face of the ever-increasing centralization of authority and control in present-day society in Britain. Leadership in rural societies was becoming leadership from without, more particularly at the hands of agricultural advisers. Secondly, the geographers were obviously reading papers in social anthropology and not in geography. Although this was inevitable in view of the topic under discussion, it did, nevertheless, prevent the symposium being in any sense a joint discussion. Professional geographers in the audience felt that in the very nature of the case they had little to contribute.

The opening speaker (or, more accurately, speakers, as Mr. H. A. Moisley read a paper on "Leadership and Innovation in the Crofting Communities of the Outer Hebrides" of which he was the joint author with Mr. J. B. Caird) had a considerable advantage. The crofting communities of the Outer Hebrides represent on one hand a remote rural society on the very fringes of centralized control, yet, on the other hand, before the days of agricultural advisers, management under such a system of partly co-operative farming tended to be primitive, no one wishing to take the onus of introducing changes and few, if any, of the shareholders had sufficient knowledge to know what changes were desirable and what was feasible. So long ago as 1919 an agricultural adviser was appointed for Lewis and resident advisers were appointed for South and North Uist in 1941 and 1954. The advisers are members of the staff of the North of Scotland Agricultural College, and this alone gives them a status which they would not have if they were regarded merely as government officials. Moreover, being permanently resident, they have become accepted as members of the community. The constant presence of such a source of advice is a very real re-assurance to the crofters embarking on some new scheme. In this way the agricultural advisers have taken over the functions of leadership and innovation in agriculture which have long been defunct. It was pointed out that in the Hebrides this natural reluctance to adopt innovations applies not only to agriculture but also to industrial and commercial pursuits. This is particularly the case with the fishing industry. The Harris tweed industry, however, provides the outstanding and perhaps the best-known example of initiative and enterprise ; but, nevertheless, mainland interests may yet swallow up the one native industry which has really flourished in the Hebrides. The lack of natural leadership in these islands can, therefore, be attributed to inhibitions due to inherent conservatism, the patriarchal influence and the tradition of equal shares. Until some means can be devised to diversify the size of agricultural units, the emergence of local natural leaders is unlikely.

No other opening speaker had such a remote and isolated society to describe, but Mr. Dafydd Jenkins's study of South Cardiganshire revealed several interesting features. He described the changes in leadership that had taken place within living memory. This Welsh community, like that of the Outer Hebrides, was basically a society organized for the

working of the land. It differed, however, from the Scottish example in that some sixty years ago social stratification was more pronounced than it is to-day. At this time the local gentry were definitely the leaders. It was they who set the standards for emulation and were the innovators of changes in agriculture. This would appear to confirm what Mr. Moisley had said about Hebridean society, namely, that diversification in social structure and in size of land-holding facilitates natural leadership. The contrast between the Anglicized, church-going squires and the Welsh-speaking, Nonconformist peasantry in Wales at the turn of this century was great indeed, and leadership in many matters fell to the squires. Two World Wars and the coming of the Welfare State eclipsed the squires, and Mr. Jenkins showed that those who took their place in South Cardiganshire were not necessarily the agricultural advisers but individuals who for some reason or other did not conform to the conventions of the existing society. For example, a man who was not a member of any chapel and went to the South of France for his holidays might be the first farmer to introduce a tractor or a combined harvester on his farm. Similarly, a farmer who was known to be in debt and had quarrelled with his minister and never appeared in chapel or frequented the local public house was likely to be the first to introduce electrical fencing on his farm. Other farmers later would follow suit. It was clear that in this society there was a sharp distinction between 'bobl y capel' (the chapel people) and 'bobl y byd' (the people of the world). Leadership and innovation after the eclipse of the squires came, as it were, from 'the odd man out' in the local social set-up, and he would inevitably belong to 'the people of this world' rather than to 'bobl y capel'.

The importance of the religious factor in social leadership was stressed also by Miss R. L. Harris, whose contribution to the discussion dealt with leadership in a border community in Northern Ireland. She emphasized the distinction between formal and informal leadership and stressed that the local clergyman was unquestionably the most important formal leader in this society. Members of the community were very reluctant to assume the role of overt leader. Miss Harris paid special attention to the relationships between the local people and such leaders. The local people tended to judge the overt leader on his or her ability to meet outsiders on equal terms, and it was only natural that Irish people would keep a very close watch on overt leaders from outside the community.

The fourth speaker, Mr. M. Kirk, whose study concerned villages in Yorkshire and Devonshire, made the audience feel the force of the impact of urban civilization on rural life in modern times to a much greater extent than any of the other speakers were able to do. One felt that Mr. Kirk's studies of these English rural communities had the advantage of emphasizing how important are the urbanizing and centralizing forces in modern English life. His title told the whole story—"The Suburban Community in the Countryside". He showed how a large number of English villages were no longer traditionally rural, because so many of their inhabitants included those who had chosen to live in the country, but derived their economic and social status from an urban setting. Village life, in consequence, has decayed. Very often the nominal leader (for example, the elected representative of the community on the rural district council) would be a retired city businessman who had come to live in the village. On the other hand, the native villagers complain that there are not enough men to form a football team, or enough women to run a successful dance. The village is clearly not what it was—in fact, according to Mr. Kirk it has ceased to exist, although its population is actually increasing. Under these conditions local leadership is at a low ebb, while initiative and innovation tend to pass to the central administration functioning through the national ministries.

The general discussion that followed the opening papers may be said to have been disappointing. There are several reasons for this. In the first place, the opening papers were specialized and presented by experts who had the advantage of considerable experience in the field. It is difficult to discuss factual data presented in this way. Furthermore, the four papers were so diverse in character that they did not lend themselves to the formulation of general conclusions, while, in addition, there was the point concerning the geographers already mentioned. One of the speakers in the open forum stressed the importance of university extension classes in rural areas in the training of leaders, while another underlined the fact, already apparent, that as centralized controls increase, local leaders decrease.

E. G. Bowen

PESTS OF STANDING CROPS

Section D (Zoology) of the British Association, during the recent meeting at Cardiff, arranged a morning session under this title since the problems raised in the attempts to understand animal population dynamics are not only interesting in themselves, but also have important applications to studies of crop pests, and some of the basic ideas are relevant to human population studies. At the plenary session of the Association on "World Food and Population", Sir Charles Darwin expressed a point of view close to that of many zoologists, but he spoke for less than five minutes. So it was fortunate that Section D had the opportunity for its own discussion, during the following morning, under the chairmanship of Mr. H. R. Hewer.

Prof. G. C. Varley, of Oxford, sought to relate the contribution of zoologists to problems of human food supply and human population. The symposium of the previous day showed the extent to which men of science are still working as if in watertight compartments. Their work is unco-ordinated, and in human affairs its impact is in opposing directions. Advances in medicine have enormously reduced human suffering and (to our satisfaction as individuals) increased our expectation of life. The reduction of mortality from disease and the increased fertility which accompanies good health have, however, increased the rate of population growth in many parts of the world.

Agricultural experts tend to accept as inevitable

a great rise in human population, and rightly claim that if given the means they can provide the extra food required—for the next forty years at least. Is it not time now to take a long view and to consider how the world population is to be stabilized? Present work is tending to make the eventual solution more difficult. If gerontologists find an easy way to prolong human life far beyond the normal span, the resultant change in the age structure of the population and its rapid increase in size might in fact precipitate a great disaster for the human race.

Many zoologists find ideas like those of Malthus still helpful in studies of animal populations. His prediction late in the eighteenth century that "misery and vice" would result if the population of the British Isles rose much further seemed so convincing that plans for a regular census of the population were made. Now, when the population has risen more than four-fold and the standard of living has also improved, how wrong poor Malthus appears! But was not his error simply his failure to foresee the industrial revolution, with its railways, road transport and steamships to bring food to these islands?

Forty years ago, Pearl fitted sigmoid logistic curves to human populations and extrapolated these to find steady limiting values. We shall not know for another century how right he was, but similar logistic curves describe very well the growth of populations of some insects, such as flour beetles, given a regular energy supply in the form of food. The population limit is reached when the birth-rate equals the death-rate; as crowding increases, the death-rate rises and the birth-rate falls. Whether the differences in human birth-rate between urban and country districts are a similar phenomenon is debatable.

The more complex problems of animal populations of two or more species living together are by no means fully understood. Consideration of the energy-flow in such systems helps in understanding them. Solar energy (about 0·1 per cent of it) is made available as human food by crop plants. Insect pests compete for this energy, and themselves serve as an energy source to their predators and parasites, which may be eaten by other animals. The fraction of available energy lost at each stage of conversion is very high. To support the greatest human population, pests must be kept down in numbers. Sir Alexander Fleck suggested that chemists have provided the method to do this and indeed they can give great help; but it must be emphasized that the problems raised are biological problems of some complexity. Animal populations in the wild and laboratory populations under constant conditions both can show violent fluctuations in numbers, the interpretation of which is still a subject for controversy. Although as yet insufficiently tested, mathematical models are available which can explain population-cycles, and some models can explain in principle why insecticides reduce the average population-levels of some pests but increase the population-levels of certain others.

Mr. D. W. Wright, of the National Vegetable Research Station, Wellesbourne, described his work on the cabbage root fly, the maggots of which feed on the plant's root system. The cabbage then suffers from water- and mineral-deficiency and is stunted or killed. Commonly about a third of the yield is lost, but this can be prevented by the careful application of suitable insecticides to the roots. However, where insecticides like DDT are used broadcast, or applied with plant fertilizers, very severe pest damage may result. This is because a high proportion of root fly eggs, clustered around the cabbage stem, are normally eaten by predatory ground beetles of the genus *Bembidion*, and low concentrations of insecticide affect these wandering predators far more than the relatively immobile maggots. Field experiments designed either to eliminate the beetles, or to concentrate them within certain areas, have shown conclusively the important role these beetles normally take in limiting the severity of damage by the cabbage root fly.

Dr. G. H. L. Dicker and Mr. R. C. Muir, of East Malling Research Station, considered some fruit pest problems. Toxic chemicals are widely used in commercial orchards and the obstacle to success is usually lack of knowledge of the biology of the pests and their natural enemies, and of the behaviour of the chemicals in the field, rather than a shortage of suitable chemicals. Regular applications of insecticides in early spring have virtually eliminated some pests like the once troublesome apple blossom weevil. Codling moth presents much greater problems. This moth lays its eggs on the young fruits of apple over a period of eight weeks or more. Very soon after hatching, the young caterpillars enter the fruits, where they can no longer be reached by insecticides. Whereas DDT suitably applied can remain sufficiently toxic over the long period of caterpillar hatching and will kill most of the larvæ before they enter a fruit, trees so treated commonly suffer severe damage from red spider mite, the predators of which are killed by DDT. The use of a further chemical spray to kill the mites was formerly effective, but the mite has now evolved resistance to a wide variety of chemicals. Special spray schedules designed to interfere as little as possible with predators of the mites are at present under investigation both in Kent and in Nova Scotia, and the results are promising.

The basis of plant resistance to insect attack remains poorly understood, but an apple rootstock resistant to woolly aphis is now available; this project took thirty years from its inception to eventual release on a commercial scale. Even so, success may only be temporary: a raspberry variety supposedly resistant to raspberry aphid was found susceptible to attack by a previously untested strain of the aphid.

A paper by Dr. R. F. Morris and Dr. C. A. Miller, of the Forest Biology Laboratory, Fredericton, N.B., Canada, on the population dynamics of some native and introduced forest insects in the Atlantic Provinces of Canada summarized long-term population changes and went a considerable way to suggest causes for them. Many of the native pests of the extensive spruce and balsam fir forests seem to have small population peaks every five to eight years, but never become common enough to cause visible damage to the trees. In contrast, the black-headed budworm has maxima on the average every seven years, and in the late 'twenties and again in the late 'forties trees were defoliated; but the population-level diminished again without the trees being killed. A study of the changes in the numbers of the hymenopterous parasites of the budworm suggests that this is an example of Nicholsonian host-parasite population oscillations. The cycles in widely separated populations in eastern Canada seem to be in phase, which suggests that some common extrinsic factor such as weather has an

effect on the periodicity. Cycles of abundance of the fall webworm can be traced from historical records so far back as 1770. The interval between outbreaks is between nine and thirteen years. In Nova Scotia the population peaks are high enough to defoliate trees whereas in New Brunswick the maxima are never so high; this curious difference in status could provide a lead to new methods of control and it is being investigated.

The spruce budworm is the major native pest of the spruce and balsam fir forests. At intervals of some forty years it has killed the trees over hundreds of square miles. The numerous species of parasites and predators which attack the spruce budworm when its numbers are low seem unable to increase quickly when the budworm outbreaks begin, and indeed seem to shun defoliated areas of the forest. The most recent outbreak began in the middle 'forties and, at its height, to save the trees more than 200 aircraft were used to spray insecticide over some 5 million acres of forest.

The introduced European spruce sawfly caused serious damage to the trees in the 'twenties. Various parasites were then imported and liberated, and some became established. For the past twenty years, these and a virus disease which was apparently introduced accidentally have kept the species below a level at which damage is significant. Time will show whether current projects for the biological control of the introduced winter moth, larch case bearer and balsam woolly aphid will eventually be successful. Only a very few years ago, biological control was regarded as possible only on oceanic islands or perhaps as an exception in California!

These papers are representative of the sort of long-term work which is now being undertaken in agricultural and forest entomology. There is clearly a great need for more applied research, but this will be easier to plan when there is more basic knowledge of the behaviour of pests and their predators and parasites, especially in relation to changes in their food supplies and population densities. G. C. Varley

GULIELMA LISTER CENTENARY

Miss Gulielma Lister, born on October 28, 1860, at 871 High Road, Leytonstone, Essex, where she died on May 18, 1949 (ref. 1), was one of those distinguished amateur naturalists of professional competence who have done so much to advance and deepen biological knowledge. She came of an intellectual Quaker stock—her father, Arthur Lister, F.R.S. (1830–1908), was a son of J. J. Lister, F.R.S. (1786–1869), and a brother of Lord Lister (1827–1912), the surgeon—and apart from a year at Bedford College she was educated at home. The course of her long life showed her to be able and industrious, economical and generous, a painstaking and accurate observer, and artistic, while her attractive personality gained her many friends. Her interests in natural history were exceptionally wide, and her detailed field knowledge of both the fauna and the flora must frequently have embarrassed specialists. Miss Lister was for many years an active member of the Essex Field Club, towards which she maintained a special affection, the Nature Study Union, and the Linnean Society, and she was twice president of the British Mycological Society. She had many calls on her artistic ability, and made notable minor contributions to botanical art in such works as her cousin F. J. Hanbury's "Illustrated Monograph of the British Hieracia" (1889–98), with its beautiful hand-coloured plates, and in addition did more utilitarian illustrations for Dallimore and Jackson's "Handbook of the Coniferae" (1923), and other publications.

Miss Lister and her father will for long be best remembered as world authorities on the Myxomycetes or Mycetozoa, an interesting, distinctive, and compact group of organisms which, as its names imply, has been approached by botanists and zoologists with a certain ambivalence. The slime moulds, now generally accepted as a fungal group, are æsthetically attractive and are of world-wide distribution. Their classification is based mainly on their macroscopic and gross microscopic characters, and as they make excellent herbarium specimens they have been widely collected and preserved so that ample material is available for their study. It is to the Listers that much credit must be given for the reasonable chance of success that now attends the attempted identification of a myxomycete from any part of the world.

Arthur Lister, like his father, a wine merchant, had life-long interests in natural history and first turned his attention to Myxomycetes in 1887, his fifty-seventh year. After a hesitant start, he applied himself to the group with vigour, and accompanied by his daughter (as amanuensis and artist, though no mean draughtsman himself) he worked over the collections of Myxomycetes at the British Museum, the Royal Botanic Gardens, Kew, and the Paris Natural History Museum, as well as de Bary's collections at the University of Strasbourg, and as a result the first edition of his "Monograph of the Mycetozoa" appeared in 1894 under the imprint of the British Museum (Natural History). After the death of her father, Miss Lister continued to study Myxomycetes for another forty years. She was responsible for the second edition of the "Monograph" (1911) and for the enlarged third edition (1925) (now unfortunately out of print and much sought after), which were lavishly illustrated in colour due to Miss Lister's generosity.

The "Monograph" is firmly based on specimens, many of which are in the British Museum (Natural History), and its background is well documented not only by the published papers of the Listers themselves and their correspondents but also in a series of seventy-four manuscript note-books (now in the possession of the British Mycological Society[2]) extending over a continuous period of sixty years, which give a fascinating picture of the day-to-day progress of the investigation, the routine of which went on uninterrupted whether at home in Leytonstone or at the Listers' seaside house at Lyme Regis. The method of notekeeping was simple. Strongly bound, thick, school exercise books of lined paper were used, and notes were entered chronologically. Entries were made giving details of collections examined, the gist of letters received and of the replies, the notes frequently being accompanied by elaborate and often highly artistic water-colour drawings—

executed directly on the lined paper, drawing paper being reserved for illustrations intended for publication. Reprints, original letters, photographs of correspondents and other matter were also loosely inserted. Separate books were devoted to material from special collections such as the Paris Museum or from important correspondents such as T. Petch (when in Ceylon). Each book when completed was indexed, and a general index to the whole series and a letter register were maintained in a folio ledger. Thus they kept their many records under continual review and easily accessible.

It was this interest in Myxomycetes which led to the long association of the Listers with the British Museum (Natural History), which Miss Lister first visited with her father around 1890 when, as mentioned above, she was helping him prepare his "Monograph". She continued her connexion with the Museum until 1939, being virtually honorary curator in charge of the Mycetozoan collection, which she helped to make the most complete and valuable in the world. With the outbreak of war, at the age of seventy-nine, the exigencies of travel made the journey from Leytonstone to South Kensington no longer possible for her.

Those of us old enough to have worked in the Botany Department of the Museum before the Second World War remember both her and her very dear friend, Miss Annie Lorraine Smith, the great lichenologist, for their ready interest, kindness and patience in helping and teaching younger workers.

Many of the Listers' specimens were deposited in the British Museum (Natural History) during their lifetime. Miss Lister bequeathed her mycological library and her Myxomycete notebooks to the British Mycological Society and her personal collection of slides and specimens to Mr. H. J. Howard of Norwich, another amateur myxomycetologist. On his death in 1957 this material was divided between the British Museum (Natural History) and the Royal Botanic Gardens, Kew.

The Linnean Society of London and the British Mycological Society arranged a meeting, held on October 28 at the British Museum, to commemorate the centenary of Miss Lister's birth and her long association with the two Societies and the Museum.

G. C. AINSWORTH
FRANCES L. BALFOUR-BROWNE

[1] Ramsbottom, J., *Nature*, **164**, 94 (1949).
[2] Ainsworth, G. C., *Trans. Brit. Mycol. Soc.*, **35**, 188 (1952).

OBITUARIES

Sir George Stapledon, C.B.E., F.R.S.

SIR GEORGE STAPLEDON, who died on September 16, was world renowned as the first director of the Welsh Plant Breeding Station at Aberystwyth; he was indeed its inspiration and the architect of its work during its formative years from 1919 up to the late 1930's.

Reginald George Stapledon was a kindly man and one whose prime interest was the human both as an individual and as part of a community. He was born in 1882, was educated at the United Services College, Westward Ho!, in North Devon, and Emmanuel College, Cambridge, where he read biology under Prof. A. C. Seward. For a period after leaving Cambridge he joined the family shipping concern, but soon returned to Cambridge, where he gained the University diploma in agriculture. In 1910 he became professor of agricultural botany at the Royal Agricultural College, Cirencester, and in 1912 went to Aberystwyth as agricultural botanist. After the outbreak of the First World War he joined the Ministry of Agriculture's Food Production Department in London. At the end of hostilities he became the first director of the newly formed Official Seed Testing Station, Cambridge, but in the summer of 1919 accepted the invitation to establish and to direct the Welsh Plant Breeding Station which was to be set up in Aberystwyth as a result of the monies given for the purpose to the University College of Wales by Sir Laurence Philipps, Bart. (now Lord Milford). Stapledon remained at Aberystwyth until the outbreak of the Second World War, when the Minister of Agriculture invited him to establish the Grassland Improvement Station at Stratford-on-Avon and to become its director. On his retirement in 1945 he joined Dunns Farm Seeds, Ltd., as scientific adviser and was soon invited to join the board of directors, a post he held until his death.

It was as director of the Welsh Plant Breeding Station that Stapledon would wish to be remembered. To him this very rightly represented the central core of his professional work. His influence, however, went far beyond Wales—indeed, it is world-wide. His was a genial personality; he was a man who worked hard and never spared himself if there was a job to do. He had the capacity also to instil into others those same personal qualities for hard work done willingly, loyally and with affection towards the leader. Stapledon was a man of ideas and of great ideals. He will be renowned in history as one of the great, and among grasslanders, as the greatest of them all. He was a notable figure in any gathering, particularly where the conversation and discussion found his interest and were to his liking.

His personal work at Aberystwyth (he himself was the cocksfoot breeder) resulted in the creation of new varieties of herbage plants, and in all essentials the types then selected are still embodied in the 'S.' varieties which are to-day widely used in Britain and in many countries overseas. It was Stapledon's creative mind which outlined the need for the study of pasture plants and to apply existing genetical and agronomic knowledge to this end. He went further, however, and insisted that there should be built up a mass of new knowledge, much of which by now has become embodied in the new science of grassland.

Stapledon was at heart a farmer. His sympathies were with the farmer and with the land. He was at once scientist, artist and humanist, a combination which was bound to culminate in an enthusiasm for applying his science—and indeed all his other talents—and bringing them to bear upon the day-to-day problems of the grassland farmer.

Early in his professional career he recognized that in grass we have a crop, the potential contribution of which to material welfare was not appreciated by the agricultural community itself, let alone by the

nation at large. This concept fired his enthusiasm, with the result that he led the British nation to plough up their derelict pastures and replace them with high-yielding leys. This process still goes on throughout Britain, which at the present time is universally acknowledged as the leader of ley farming techniques among the countries of the world.

William Davies

Dr. D. Chatterjee

Dr. Debabrata Chatterjee, superintendent of the Indian Botanic Garden, Sibpur, Calcutta, was shot dead at point-blank range on September 24 by one of his subordinates, who, having committed this utterly wanton and senseless crime, turned the gun on himself and successfully brought his own life to an end. It appears that the assassin aspired to a post in the Botanical Survey of India, and although he did not possess the necessary qualifications he fancied that Dr. Chatterjee was not active enough in furthering his claims. Homicidal mania, inflamed by an insane sense of injustice and frustration, was responsible for the death of one of India's leading botanists at the early age of fifty.

Dr. Chatterjee received his early botanical training at the Presidency College, Calcutta, obtaining his M.Sc. in botany in 1937. From Calcutta he proceeded to the University of Edinburgh, where he worked for two years under the late Sir William Wright Smith. He obtained the Ph.D. degree for a thesis dealing with endemism of Indian plants. On his return to India he worked for a time in the herbarium at Sibpur and then went to Burma as a lecturer in botany at Mandalay College. He escaped to India when the Japanese invaded Burma in 1942 and lectured at the Cotton College, Gauhati, Assam, for four years. He became botanist for India at the Royal Botanic Gardens, Kew, in 1946, and in 1949 was appointed to the post of systematic botanist at the Indian Agricultural Research Institute, which he held for six years. He succeeded Dr. K. Biswas in 1955 as superintendent of the Indian Botanic Garden.

Dr. Chatterjee's botanical interest lay mainly in the taxonomy of Indian and Burmese plants, and he published papers in a number of journals including the *Kew Bulletin*, *Hooker's Icones*, *Nature* and several others. Since leaving Kew he had never really had the opportunity of developing his undoubted taxonomic ability. For part of the time he had to work without an adequate herbarium or library, while during the past few years he had been overwhelmed with the numerous details inherent in the administration of the Botanic Garden. Even so, his loss will be severely felt in India, where there is a conspicuous shortage of competent taxonomists.

At Kew he will be remembered as a congenial colleague who did valuable work for India during the period he worked there.

He is survived by his aged parents and by his only daughter, to whom our sympathy is due. His wife died some years ago.

N. L. Bor

NEWS and VIEWS

Nobel Prize for Medicine

The Nobel Prize for Medicine, amounting to about £15,000, has been awarded jointly to Sir Macfarlane Burnet, director of the Walter and Eliza Hall Institute for Medical Research and professor of experimental medicine in the University of Melbourne, and Prof. P. B. Medawar, Jodrell professor of zoology and comparative anatomy in University College, London. Both recipients are well known for their work on acquired immunological tolerance, which has initiated a new era in experimental biology and medicine. (See p. 376 of this issue.)

A.R.C. Institute of Animal Physiology, Babraham : Dr. R. Keynes, F.R.S.

A number of new appointments to senior posts at the Agricultural Research Council's Institute of Animal Physiology at Babraham, near Cambridge, has recently been made.

Dr. Richard Keynes has been appointed head of the Physiology Department. He succeeds Dr. I. de Burgh Daly who was head of this Department as well as being director of the Institute. Dr. Keynes's scientific work has mostly been done in Cambridge, but, during the War, he worked for five years with the Navy on asdic and radar. His best-known researches are concerned with the movement of ions in nerve and muscle and the origin of the discharge in electric fish. He measured the quantities of radioactive sodium and potassium which cross the surface membrane of a single nerve fibre during the passage of an impulse. More recently he has studied the movements of these ions against concentration differences during recovery, and has become interested in the metabolism of potassium in the whole animal. He has been a member of the editorial board of the *Journal of Physiology* since 1954 and is now chairman. Dr. Catherine Hebb has become head of a Sub-Department of Chemical Physiology.

Dr. T. Gillman

Dr. Theodore Gillman succeeds Sir Alan Drury as head of the Experimental Pathology Department. Sir Alan went to Babraham in 1952 and established this Department as an active centre for work on cell surfaces, immunity, and blood groups in cattle and sheep, with especial reference to genetics. Dr. Gillman graduated in the University of the Witwatersrand and became lecturer in clinical pathology. He was appointed professor of physiology in Durban in 1951, but he has not been confined by the title of his department, and has worked, not only on gastric physiology, but also on iron metabolism, malnutrition, neoplasms, and liver disease. Recently he has been interested in tissue reactions in wound healing, the ageing of arteries and the transplantation of tissues. Dr. Gillman is an energetic person ; while he was in Durban he built up a large and active department from nothing, replanning the architecture and organizing courses in physiology, biochemistry and pharmacology, and wrote many scientific papers.

Dr. G. D. Greville

Dr. G. D. Greville has become head of the Biochemistry Department in succession to Sir Rudolph Peters, who went to Babraham in 1954 and built up a distinguished staff of biochemists. Dr. Greville graduated in Cambridge and then worked during 1932–37 at the Middlesex Hospital in London. He was biochemist to Runwell Hospital for seven years, and returned to the Biochemical Department in Cambridge in 1944. He has worked in many fields, including glucose tolerance, carbohydrate chemistry, blood coagulation and mental disorder, but his main interest has been in tissue metabolism. He was responsible for an early demonstration of the uncoupling effect of nitrophenols and has studied the effects of various metabolic ions. Recently he has published an interesting series of papers on the metabolic changes associated with the swelling of mitochondria.

Dr. Marthe Vogt, F.R.S.

Dr. Marthe Vogt has become head of a new Pharmacology Unit at Babraham. Her early work was done in Berlin under her famous father, Dr. Oskar Vogt, and Profs. Neuberg and Trendelenberg. She came to Britain in 1935 and showed, with Dale and Feldberg, that acetylcholine is liberated at motor nerve endings in voluntary muscle. She worked with Verney in Cambridge during 1935–39 on renal hypertension in dogs. From there she went to the laboratories of the Pharmaceutical Society in London and started work on the adrenal cortex. She showed that the output of hormones in the blood was large compared with the amounts stored in the gland and that adrenaline increased the rate of liberation. She still works on the adrenal cortex and is one of the leading authorities on the subject, but she has also done distinguished work in other fields. In 1946, she followed Gaddum to Edinburgh and became interested in adrenaline and noradrenaline. It was her work, published in 1954, which convinced the world that these catecholamines are likely to play some part in the physiology of the brain, since they have a specific distribution and are affected by such factors as the injection of drugs. This has led to a great deal of work on the biochemical mechanisms by which drugs may cause tranquillity or arousal.

The National Institute of Sciences of India : Honorary Fellows

The following have been elected Honorary Fellows of the National Institute of Sciences of India: Prof. D. Bovet (director of therapeutic chemistry, Istituto Superiore de Sanità); Sir John Cockcroft (Master of Churchill College, Cambridge); Dr. W. Shockley (Shockley Transistor Corporation, Mount View, California); Prof. E. C. Titchmarsh (Savilian professor of geometry, Oxford).

The NATO Summer Schools Programme

The North Atlantic Treaty Organization was created as a defensive organization, and is usually thought of only in a military context. The changing nature of the challenge to NATO countries during recent years, however, has caused NATO to widen its outlook, and in 1957 a Science Committee was established to promote scientific co-operation between NATO countries, and among the schemes adopted is the NATO Advanced Study Institutes Programme. NATO spent 100,000 dollars in 1959 and 200,000 dollars in 1960 on these 'summer schools'. Grants to individual schools varied between 3,000 and 45,000 dollars, normally being between 10,000 and 15,000 dollars. The grants are used to cover overhead expenses, to facilitate publication of the proceedings, and a considerable part is usually available to subsidize foreign visitors. In 1959 all five schools were on subjects in physics, and in 1960 nine of the fifteen schools were also in physics. Among the other schools in 1960 was a course at the Royal College of Science and Technology, Glasgow, on food science, and another at the Max-Planck-Institut für Tierzucht und Tierernährung at Mariensee dealt with methods of improving productivity with livestock. Both these topics range widely over a number of academic disciplines, and the lecture courses were arranged to survey the whole field. Rather different in intention were the courses on crystallography at the Manchester College of Science and Technology, and on protein analysis at the Medizinische Forschungsanstalt der Max-Planck-Gesellschaft at Göttingen, both of which were highly practical in outlook. Attendance at the schools was not restricted to people from NATO countries.

Naturally, the NATO grant does not cover all costs, but it often enables the quality of the summer schools to be considerably improved by inviting foreign scientists. It is expected that 300,000 dollars will be available in 1961 for the Advanced Study Institute Programme. Courses already arranged for 1961 include the following: theoretical physics (Dr. L. W. H. Trainor) at Montreal; theoretical chemistry (Prof. C. A. Coulson) at Oxford; use of computers in engineering problems (National Laboratory of Civil Engineering, Lisbon) at Lisbon; solid state theory (Prof. W. Dekeyser) at Ghent; medical documentation (Dr. O. Nacke) at Bielefeld. Anyone interested in organizing such a course, and requiring financial assistance from NATO, should write to the Office of the Science Adviser, NATO, Place du Maréchal de Lattre de Tassigny, Paris 16e, before December 15.

Safety in Mines Research

The annual report of the Safety in Mines Research Establishment of the Ministry of Power for 1959 contains sections devoted to explosives and blasting devices, explosion hazard, rescue apparatus, fire hazard, engineering and metallurgical research, investigation of mining incidents and examination of equipment after mine service, dust measurement and the pneumoconiosis hazard, and testing services (Pp. 66+4 plates. 4*s*. 6*d*. net. London: H.M. Stationery Office). Among the most interesting topics of the report are those concerned with firedamp roof-layers, investigation of incidents and pneumoconiosis. During the past two years problems connected with the formation and movement of firedamp roof-layers have been intensively studied and a parameter, the layering number, has been developed which will be of importance in the work of ventilating engineers. A new section, the Incidents Section, has been established within the organization to co-ordinate the work concerned with investigation of actual incidents and to provide men specially trained in scientific aspects of mine disasters, particularly actual underground explosions and fires. Although the pneumoconiosis research has followed broad lines similar to those of previous years, much interest has

been directed towards the development of a gravimetric sampler for measurement of respirable dust, and the opinion is expressed that measuring the mass concentration of respirable dust may prove more useful and convenient than the present practice of measuring particle-number concentrations. Altogether a variety of topics is covered within the sections of the report and many of these are of scientific and technological interest to a wide range of industries in addition to the mining industry.

The International Journal of Heat and Mass Transfer

The wide application of heat and mass transfer, including almost every form of engineering, chemistry and physics, has made it inevitable that much valuable information has hitherto appeared in specialized journals which pass unnoticed by workers in other fields, who might well find use for such data. The very large number of papers now published indeed makes it impossible to examine all the journals containing such subject-matter. The addition of a new monthly journal, published by the Pergamon Press, and entitled *The International Journal of Heat and Mass Transfer*, will be welcomed by all engaged in such work (1, No. 1; June 1960. Pp. 114. Subscription rates: (*A*) for Libraries, Government Establishments, Research Laboratories, etc., £7 (20 dollars) per vol.; (*B*) for individuals who place their orders directly with the publisher and certify that the journal is for their personal use, £5 5*s*. (15 dollars) per annum). Six distinguished editors drawn from Great Britain, the United States, U.S.S.R. and Germany, assisted by some fifty advisers representing major academic and industrial concerns from all over the world, should ensure a truly international journal with a succession of papers of high standard. The first issue contains an editorial article and ten papers, two of which are in German, one in French, the remainder in English; all papers have an abstract in English, French, German and Russian. There is also a "Bibliography of Heat Transfer", presumably of publications written in the past few years only, though this is not stated. Research workers already familiar with advanced concepts will find the contents of the most value. It is to be hoped that the editors will from time to time include fundamental but more elementary articles for the benefit of less erudite students, such as those in their first year of Ph.D. work.

Bibliography of Research at Oak Ridge National Laboratory

A list of articles by members of the staff of the Oak Ridge National Laboratory (operated by the Union Carbide Corporation for the United States Atomic Energy Commission) published during 1959 in technical journals has been issued by the Laboratory, and requests for reprints where available, as indicated by the prefix *R*, should be addressed to the Central Research Library at the Laboratory (Pp. v + 84. Oak Ridge, Tennessee: Oak Ridge National Laboratory, U.S. Atomic Energy Commission, 1960). The articles are arranged alphabetically by author under nine divisions: biology; chemistry; general; health physics; instrumentation; mathematics; metallurgy and materials; physics; and technology. There is an accompanying list of reports issued by the Laboratory, and these, except when indicated as "Not for sale", should be ordered through the Office of Technical Services, Department of Commerce, Washington 25, D.C. A third list, similarly arranged, records the titles of papers presented at scientific meetings, and requests for information regarding these papers should be addressed to the authors concerned. Titles of eighteen theses completed at the Laboratory during the year are given in a fourth list, alphabetical by author, and finally there is a list of sixty-eight inventions disclosed during the year.

Research into Electricity Supply

As a postscript to an article on the supply of electricity in Great Britain, Arthur Palmer suggests unified areas where research could be carried out (*Research Applied in Industry*, 13, No. 9: September 1960). These include investigations into fundamental questions of electricity production and use: for example, ways and means of escaping the limitations of the thermodynamic cycle and methods of solving the outstanding energy storage problem; investigations into reductions of cost in all the fields of generation, transmission, distribution and utilization—this is primarily a scientific and engineering matter, but it must occasionally take account of psychology or even sociology; investigations into techniques for reducing the social nuisance of electrical processes—in an island packed with more and more human beings demanding simultaneously the often mutually contradictory ends of higher and better standards, this is no easy task; and investigations into the possibility of maintaining human interest in an industrial environment which when ideally organized and arranged will record the almost effortless glide of electrons from genesis to consummation.

Poison Sprays and Wild Life

A Joint Committee of the Royal Society for the Protection of Birds and the British Trust for Ornithology has been formed under the chairmanship of Mr. S. Cramp to study the effect of toxic chemicals on birds. The Committee is anxious to obtain evidence of kills of birds due to agricultural chemicals used in sprays or in the form of seed dressings. The basic information needed is the date and locality of the kills, the species and number of birds affected and the chemical used. The Committee would appreciate prompt notification of birds the death of which is thought to be due to agricultural chemicals, so that if necessary corpses may be collected for chemical analysis. Information should be sent to the secretary of the Committee, Mr. P. J. Conder, Royal Society for the Protection of Birds, 25 Eccleston Square, London, S.W.1.

Insulin

A recent issue of the *British Medical Bulletin* deals with insulin in its varied aspects (16, No. 3; September 1960). Prof. Charles H. Best describes his pioneer work with Banting and developments which have occurred during the past forty years. This is followed by an account by Dr. F. Sanger of the chemistry of insulin based on his Nobel Prize Lecture. Other articles include one by Dr. Ieun Harris on the chemistry of pituitary polypeptide hormones; methods of insulin assay by G. A. Stewart; insulin antibodies by Dr. P. H. Wright; the action of insulin on carbohydrate metabolism by Dr. R. B.

Fisher; fatty acid metabolism by Drs. S. J. Folley and A. L. Greenbaum and the mechanism of the action of insulin by Dr. P. J. Randle and Prof. F. G. Young. Prof. F. G. Young has acted as scientific editor of this issue.

Inhibition of Development in Rust Fungi

D. J. SAMBORSKI and F. R. Forsyth have reported on the inhibition of the development of rust fungi, on detached wheat leaves, by various metabolites, antimetabolites and enzyme poisons (*Canad. J. Bot.*, 38, 467; 1960). This is part of a series of investigations in which attempts are being made to correlate changes in the reaction of the pathogen with changes in endogenous levels of substrate in the host. In the experiments, detached leaves of Little Club wheat were floated on solutions containing benzimidazole and the compound being tested. The effects of purine and pyrimidines, vitamins, amino-acids, carbohydrates and enzyme poisons were examined. A number of these compounds inhibited leaf and stem rusts at concentrations that were not injurious to the host. Of the purines and pyrimidines tested, thymine and the analogue azathymine were the only effective inhibitors. The antivitamin oxythiamine was inhibitory, the inhibition being completely reversed by thiamine. A few natural amino-acids, notably histidine, isoleucine, methionine and serine, inhibited rust development. The inhibition was reversed by glycine in all cases except with serine. Amino-acid analogues, particularly canavanine, ethionine and *p*-fluorophenylalanine, were very good inhibitors, the inhibitions being reversed by comparable levels of arginine, methionine and phenylalanine, respectively. The carbohydrates lyxose, xylose, sorbose, and all the sugar alcohols tested were effective inhibitors of rust development. Of the enzyme poisons tested, sodium fluoride and sodium azide differentially inhibited rust growth.

The Gairdner Foundation: Awards

AWARDS totalling 30,000 dollars for medical work in arthritis and heart disease have been made by the Gairdner Foundation to four American and two British medical scientists as follows: Prof. John H. Gibbon, jun., professor of surgery and director of surgical research, Jefferson Medical College, Philadelphia; Prof. William F. Hamilton, professor of physiology, University of Georgia School of Medicine; Dr. Karl Meyer, dean of medicine at Columbia University, New York; Prof. Arnold R. Rich, Baxley professor emeritus of pathology, Johns Hopkins University; Prof. J. McMichael, professor of medicine, University of London; Prof. J. H. Burn, recently professor of pharmacology, University of Oxford. The awards will be worth 5,000 dollars each, and are prizes for achievements rather than for the support of future research.

U.S. Society for the Study of Development and Growth

THE following were elected officers of the U.S. Society for the Study of Development and Growth for the year November 1960–November 1961: *president*, Prof. William P. Jacobs (Princeton University); *secretary*, Prof. Armin Braun (Rockefeller Institute); *treasurer*, Prof. H. Clark Dalton (New York University). The other members of the executive committee are: Prof. Clifford Grobstein (newly elected), and Profs. Arthur Galston and Dietrich Bodenstein.

The Association of Clinical Biochemists

THE Association of Clinical Biochemists has elected the following officers for the session 1960–61: *president*, Dr. C. P. Stewart; *chairman*, Dr. A. L. Latner; *honorary treasurer*, Dr. R. Gaddie; *honorary editor*, Mr. H. Varley; *honorary secretary*, Dr. J. H. Wilkinson (Westminster Medical School, Horseferry Road, London, S.W.1).

Announcements

MR. A. D. MCKNIGHT, executive commissioner of the Australian Atomic Energy Commission, has been elected chairman of the Board of Governors of the International Atomic Energy Agency for the next year.

THE eleventh session of the United Nation's Educational, Scientific and Cultural Organization is to be held at Unesco House, Place de Fontenoy, Paris, during November 14–December 13. The main subject for discussion will be International Co-operation for Oceanographic Research.

AN all-day session of the Welsh Soils Discussion Group will be held in the Department of Geography and Anthropology, University College, Aberystwyth, on November 16. The theme will be: "Glaciation in Wales as related to Soil Profile Development". Further information can be obtained from Mr. James A. Taylor, Department of Geography, University College of Wales, Alexandra Road, Aberystwyth.

A SYMPOSIUM on "Inorganic Polymers" is being sponsored by the Chemical Society, and will be held at the University of Nottingham during July 18–21, 1961. Further information can be obtained from the General Secretary, Chemical Society, Burlington House, London, W.1.

THE 1960 meeting of the American Association for the Advancement of Science will be held in New York City during December 26–31. Further information can be obtained from the director of public information for the meeting, Sidney S. Negus, Medical College of Virginia, Richmond, Virginia.

THE Plant Phenolics Group is holding a one-day meeting on "The Stereochemistry of Natural Phenolic Compounds" at the Department of Engineering, University of Bristol, on December 16. Further details can be obtained from the Honorary Secretary of the Group, Low Temperature Research Station, Downing Street, Cambridge.

THE third international conference on "Analogue Computation" will take place in Belgrade during September 4–9, 1961. The conference is being organized by the International Association for Analog Computation. Further information can be obtained from L. Radanović, Yugoslav Committee for Electronics, Telecommunications, Automation and Nuclear Engineering, Tarazije 23/VII, Belgrade.

DIAMOND PHYSICS

A CONFERENCE on diamond physics was held during September 22–23 at the J. J. Thomson Physical Laboratory, University of Reading, under the auspices of the Institute of Physics and the Physical Society. More than a hundred delegates attended, and twenty-one papers were presented, most of which originated in Great Britain, but contributions were also received from the United States and one from Stockholm. Most of the contributions were experimental; two theoretical papers on related topics were those of P. Ewald (United States) on the electron density of diamond and of H. Bolton and H. Clark (Newcastle) on the nature of the bond orbitals. It was generally agreed that the electron density is much less concentrated than the word bond might imply, but it still remains very difficult to account theoretically for the intensity of the (222) X-ray reflexion observed in some specimens.

Two papers were devoted to synthetic diamonds. That on their production by E. Lundblad (A.S.E.A., Stockholm) compared different methods of synthesis using various catalysts and conditions of temperature and pressure but no direct transition of graphite to diamond has yet been achieved. The results therefore confirm these of the General Electric Co. (United States).

G. Kennedy (United States) and others, however, pointed out that they were convinced that the pressures at present quoted on the Bridgman scale were about 30 per cent above the true value at pressures greater than 25,000 atm. Consequently diamond formation occurred considerably below the region indicated by the Simon graphite-diamond equilibrium curve, which therefore needed revision.

The diamonds produced synthetically may have either type I or type II characteristics according to the method of production.

The other paper, by S. Tolansky (University of London), on optical and interferometric studies on the surface characteristics of diamonds compared the synthetic products from several different sources. A wide variation in crystal perfection was observed, some batches of specimens consisting of 'hopper-type' crystals whereas other batches were relatively perfect. Growth spirals were detected on specimens from one batch.

There were several contributions on semi-conducting diamonds. H. Farnsworth and J. Marsh (United States), using normal incidence on the (100) face, showed that the electron diffraction pattern below 350 eV. contained no half-integral order surface grating beams, thus indicating that the positions of the atoms in the surface monolayer are not displaced from their 'normal' positions as for silicon and germanium. Changes in the intensity of the diffraction pattern on heating treatment are interpreted in terms of variations in adsorbed oxygen, but there was some disagreement on details of the interpretation.

F. C. Champion and J. Male (London) compared the luminescence excitation spectrum of a semiconducting specimen with its absorption spectrum and showed that the former method sometimes gave information absent from absorption data. For example, it showed quite clearly a level agreeing with an acceptor-level at 0·35 eV. from the valence band. Measurements of the anisotropy of the magnetoresistance in three oriented crystals of p-type semiconducting diamond by P. J. Kemmey and E. W. J. Mitchell (Reading) were compared with calculations based on the approximate model of two warped and one spherical energy band surface, degenerate at $\mathbf{K} = 0$.

Contributions to the study of graphitization were made by M. Seal (United States) and by T. Evans and C. Phaal, and Evans and H. Sauter (Reading), the two latter emphasizing the aspect of etch-rate determination and etch-pit orientation on diamond surfaces. It was shown that trigons oriented such that the apices of the triangles on the octahedral face were pointed towards the sides of the face, as in naturally occurring trigons, could be produced by etching with an oxygen and water vapour mixture above about 800° C. Below that temperature the trigons had the usual etch orientation with sides of the trigons parallel to the sides of the crystal face. High-temperature and high-vacuum graphitization experiments on diamond were also described by V. Howes (Reading).

Experiments on irradiation damage to diamonds by electrons of energies up to 2 MeV. were described. Changes in the optical absorption of a type IIa diamond near 2 eV. were compared with the theoretically expected rate of defect production and agreement below 1 MeV., obtained if the displacement energy is $E_d = 80$ eV. Corresponding measurements on the change of resistivity of a IIb diamond with radiation dosage were in agreement with the absorption data up to 1 MeV., but above this energy C. Clark, P. J. Kemmey and E. W. J. Mitchell (Reading) found poor agreement, the explanation of which is uncertain. D. Palmer and C. D. Clark (Reading) showed from corresponding absorption changes with temperature that complex annealing processes occurred indicating a wide range of activation energies. Tentative models of the various annealing stages over the range 150°–800° C. were proposed. It was suggested during discussion that the interpretation of these experiments would be far more definite if in the first instance the energy of the bombarding electrons was confined to a value just above threshold (say, 0·5 MeV.), so that only one predominant type of defect was produced, namely, close vacancy-interstitial pairs. The number of possible activation-energies required to interpret the annealing data would then be a minimum and the significance of the present results, obtained at bombarding energy up to 2 MeV., could be more fully appreciated.

A two-phonon process was suggested by J. R. Hardy and S. Smith (Reading) to account for specimen-independent absorption between 3·75 and 7·5μ. It confirmed that long-range forces are far less important in diamond than in silicon or germanium. Phonons and also excitons were invoked by F. C. Champion and J. Male (London) to explain specimen-independent broad bands in the luminescent excitation spectrum of all types of diamond except type IIb at energies greater than 5·45 eV., but bands at 5·25, 5·36 and 5·39 were attributed to some defect other than nitrogen.

J. Male and J. R. Prior (London) also reported the first examples of fluorescent emission in the ultra-violet from diamond at energies near 5·1 and 5·3 eV.

The growing interest in silicon carbide was shown by four papers on practical aspects involving various mechanical properties such as friction and wear of diamond and silicon carbide, by C. Brookes, by D. R. Miller, by L. M. Fitzgerald and by F. Field and N. L. Hancox, all from Cambridge. The steady improvement in the purity control of silicon carbide was described by W. F. Knippenberg (Holland). Using as starting material cubic silicon carbide prepared by decomposition of chlorosilanes, the total content of foreign atoms, which were mostly chlorine, could be reduced to less than 10^{16} cm.$^{-3}$. Using such pure material, H. Daal, W. Knippenberg and J. D. Wassher measured the Hall constant and the resistance of silicon carbide from 80° to 1,400° K. Much lattice imperfection is indicated since the number of acceptors and donors exceeds the number of chemical impurities by an order of magnitude. Occupying as it does a key intermediate position between silicon and diamond, all the properties of silicon carbide are of great interest and importance. However, because of the different possible atomic arrangements such as cubic and such polytypes as 4H and 6H in the hexagonal form, the interpretation of the optical and electrical properties of silicon carbide is complex. D. Hamilton, W. J. Choyke and L. Patrick (United States) have examined the optical absorption and photoluminescence of 4H silicon carbide, extending earlier work on the 6H polytype. A characteristic edge luminescence was observed in the pure 4H crystals and parts of the spectrum were found to have photon energies greater than the energy gap of polytype 6H. Corresponding absorption experiments showed that the 4H energy gap exceeds the 6H energy gap by 0·25 eV. The transitions are indirect and exciton absorption is observed.

The impression gained from the Conference was that although diamond physics is still in its infancy, sufficient experiments have now been performed over a wide range of properties and techniques to indicate that a relatively few well-chosen experiments, such as the investigation of radiation damage close to the threshold energy, should throw real light on fundamental problems in solid state physics. As Prof. R. W. Ditchburn pointed out at the beginning of the Conference, the unique property of diamond is its stability and the simplicity of its composition. These striking advantages compared, for example, with the alkali halides, as set out in a conference on crystal luminescence held two weeks earlier in Turin, seem to me far to outweigh the relative intractability of diamond as a material in that it prevents the overwhelming flood of experimental data which would undoubtedly ensue if simple methods of 'doping' diamond were available. Diamond physics is on an orderly march which should lead to a real advance in our understanding of solid state physics.

Advantage was taken of the opportunity provided by the Conference to present the Duddell Medal to Prof. R. V. Jones, who then spoke on some developments of the optical lever. In an excellent lecture, enjoyed by all, Prof. Jones described in particular the development of the optical lever in the past ten years up to the present stage when the performance approaches the limit set by the statistical fluctuations of photons in the light beam. Applications covered the evaluation of the thermal fluctuation limit for galvanometers, the detection of the change of linear momentum in a beam of light after refraction, and the development of a sensitive infra-red detector based on linear thermal expansion. The method failed to detect any deviation of a beam of light in an inhomogeneous transverse magnetic field of mean value 8,000 oersteds, although a change in the velocity of light of about 70 μsec.$^{-1}$ should have given a deviation equal to the r.m.s. error.

F. C. Champion

THERMAL MOTION IN CRYSTALS AND MOLECULES

THE fifth international congress of the International Union of Crystallography which was held recently in Cambridge was followed by two symposia, one of which was devoted to papers on Thermal Motion in Crystals and Molecules. This symposium lasted for two days, August 22–23, apart from an introductory lecture which was given during the main congress in the previous week. It consisted of five invited papers and thirty other contributions, abstracts of which had been published in advance of the meeting by the International Union of Crystallography.

In the early days of crystallographic studies by X-ray diffraction techniques, thermal motion was a disturbing factor for which rather empirical correction had to be made, by means of the familiar Debye–Waller theory, before the crystallographer could make a crucial comparison of his experimental intensity results with deductions from any postulated structural model. Since then the increasing accuracy of measurements and ease of interpretation have permitted the process to be largely reversed and experiment now allows a detailed assessment of atomic motions to be made and analysed into various types of vibration. Investigators are no longer restricted to the use of X-rays for electrons, and neutrons are now being widely used in support. Moreover, further theoretical work on the various scattering processes and improvements in experimental techniques have played their parts in increasing the interest in this field of work. During the past few years it is particularly noteworthy that rather empirical descriptions of atomic motions are being superseded by much more comprehensive descriptions of co-operative motions of molecules and crystals as a whole. To a considerable extent, interest has been fostered by the increasing availability of computing machines and programmes able to analyse the experimental results in terms of the many parameters needed for a full description of thermal motion.

Although receptive of any aspect of thermal motion in crystals and molecules, the symposium was aimed at providing discussion of three particular topics: first, the study of the elastic and inelastic scattering of X-rays and neutrons by solids, as a

source of information on the amplitudes and frequencies of motion in crystals and their dependence on temperature; secondly, the use of electron diffraction measurements to study molecular motion in gases; and thirdly, data on residual motion in crystals at low temperatures. The introductory lecture by Prof. J. C. Slater served as a general lecture to the whole congress and was entitled "The Interaction of Mechanical and Electromagnetic Waves in Crystals". While summarizing the more conventional aspects of the scattering of radiation by phonons in crystals, this lecture surveyed the interactions over a very wide range of frequency, and included an account of recent work on the explanation of ferroelectric transitions from the point of view of lattice dynamics. The treatment of Cochran, whereby a ferroelectric transition is emphasized as being a limit of stability against a particular mode of vibration, was shown as a development of the much earlier work of Huang and others on anomalous dispersion in the infra-red region, where a transverse electromagnetic wave interacts with transverse mechanical oscillations in a crystal.

The main symposium began with an invited paper by Dr. D. W. J. Cruickshank, who discussed, chiefly from a theoretical point of view, the determination of atomic vibration amplitudes from X-ray diffraction data, particularly in molecular crystals where the motions are anisotropic. For each atom a vibration tensor with six components can be deduced and these tensors can then be combined to give a picture of both rigid-body vibrations of the molecule as a whole and of internal vibrations within the molecule. At room temperature the latter are relatively small, but they become of greater importance as the temperature is reduced. It was emphasized that X-ray diffraction data alone are not sufficient to give an unambiguous solution, and it is necessary to employ spectroscopic evidence as well in order to distinguish, for example, between internal twisting vibrations and angular oscillations as a rigid body. Investigations concerning the perchlorate ion in perchloric acid monohydrate ($H_3O.ClO_4$) and of ethane were described as examples of the essential part played by spectroscopic data in the analysis of the various motions. The following, complementary, paper by Dame Kathleen Lonsdale surveyed the problems from a more practical point of view in the light of much experimental information accumulated by the author and her colleagues at University College, London. In practice, before true thermal vibrations can be studied, allowance has to be made for zero-point energy, structural disorder and bonding anisotropy. Measurements at reduced temperature and parallel studies with X-rays and neutrons may be necessary in order to secure unequivocal results. The partition of the total thermal motion among internal and rigid-body vibrations was discussed, taking urea, hexamine, naphthalene and anthracene as examples. In the latter case where the directions of the principal axes of atomic vibration are not fixed by crystal symmetry, wide discrepancies in their specification from different, seemingly accurate, sets of results were found. It would seem to be well established that there is still a considerable need for data with improved accuracy, more free from both random and systematic errors, if the detailed conclusions which are drawn from structural analyses of this type are to be justified.

These two general review papers were followed by several descriptions of structural analyses which depended on the principles previously enunciated, illustrating in the main the relation between atomic motion and the environment of an atom, both within its own molecule and among its neighbours, and with some attention being directed to developments of experimental technique. Increasing attention is certainly being given to measurements at low temperature, but there are still only a few substances for which a detailed analysis has been made at more than one temperature. The value of supporting evidence from other physical methods of analysis, such as specific heats, nuclear magnetic resonance and spectroscopy, is very great.

Both Dr. Cruickshank and Dame Kathleen Lonsdale referred to the information on molecular motion which could be obtained from work on the diffuse inelastic scattering, as distinct from the elastic Bragg peaks, and this theme was taken up in more detail by later contributors. Papers by Dr. W. Cochran and Prof. W. Hoppe described the theoretical calculation of the diffuse scattering from molecular crystals, pointing out the relative significances of the displacements due to translation and rotational motion, and distinguishing between the enhancement of diffuse scattering in the neighbourhood of reciprocal lattice points and that over extended areas. Several succeeding contributions described the experimental verification of these ideas and their value in structure determination. A paper by Dr. M. L. Canut illustrated how experimental measurements of the shape and location of the extended regions of diffuse scattering were in good agreement with calculations made from the shape and orientation of the molecules for substances such as hexamine, pentaerythritol and naphthalene. A related contribution from Drs. E. Sandor and W. A. Wooster emphasized that the detailed interpretation of the diffuse scattering might be carried out accurately enough to be of value in structure analysis. Particularly for planar molecules, the orientation in the structure of a molecule of known shape could be predicted and a molecular Patterson function could be calculated.

In a group of papers on electron diffraction work on gases, it was evident that the greatly increased experimental accuracy which can now be attained has stimulated interest in more detailed work on the diffraction process and the force fields in molecules. Prof. Y. Morino discussed the exact relation of the experimentally determined quantities—the mean atomic distance and the mean square vibration amplitudes—to the actual equilibrium distance and the detailed molecular field. Prof. O. Bastiansen and his colleagues showed that certain linear molecules may appear to be bent on account of vibrations perpendicular to the bond, because the longer interatomic distances within the molecule appear to be shorter than expected from a summation of observed bond distances. Carbon suboxide was shown to be a case where it is difficult to distinguish between a linear molecule with large out-of-line vibrations and a bent equilibrium configuration. One was impressed by recent improvements in experimental techniques; for example, K. Hedberg described how it was now possible to measure the increase with temperature of the vibration amplitudes in phosphorus trichloride, in fair agreement with predictions from spectroscopic data. In discussions of these electron diffraction papers, attention was directed to the importance of using complex scattering factors, reliable values of which are now becoming known and listed.

The influence of atomic vibrations on measured values of lengths of bonds is not, of course, limited to electron diffraction work, and a paper by H. Levy discussed this problem in relation to precise structure refinements by X-ray and neutron diffraction methods. It was shown how the apparent interatomic distance for a pair of atoms depended on whether or not their individual thermal motions were linked or independent. Any attempt to deduce the equilibrium distance of separation, as distinct from the centroid separation, depends on reaching a precise knowledge of the atomic vibrations after making measurements at various temperatures, followed by an extrapolation and allowance for zero point motion. In discussion it was made clear that whenever corrected distances are given it is very essential to specify on what assumptions the corrections have been made. The effects are of particular importance when the motions of hydrogen atoms are being considered and are of especial interest in work on neutron diffraction. This paper, in fact, formed part of a session which was devoted to the contribution of neutron methods to our knowledge of thermal motion, which Dr. W. Cochran opened with a discussion of the great value of measurements of energy distributions of scattered neutrons in a review of recent work on lattice dynamics by neutron spectroscopy at Chalk River. Of particular interest were an extensive series of precise measurements of the dispersion relation, between frequency and wave-number, for the acoustic vibrations in single crystals of lead. In order to interpret the results it is necessary to assume that long-range forces are important in the solid and it is shown that their range becomes less as the temperature is increased. From the widths of the peaks in the neutron-energy spectrum it is possible to deduce the life-time of the phonon vibrations. In a further comprehensive set of measurements the lattice dynamics of the alkali halides and of lithium hydride were investigated. As an example of the contribution of neutron methods to disentangling the effects of thermal vibration and bond anisotropy, a paper given by Dr. R. S. Calder described concurrent neutron and X-ray work on lithium hydride.

In the final session of the symposium, Prof. I. Waller described some recent theoretical work on the frequency distribution and dispersion relations for alkali halides at low temperatures, with particular reference to the approximations which have been made in calculating the form of the zero-point energy vibration amplitudes. The conclusions are in good agreement with results of diffraction experiments. In an interesting survey of a wide range of experimental data, F. H. Herbstein examined the values of Debye temperature determined for cubic crystals by methods such as specific heat and elastic constant measurement, as well as by diffraction studies at one or several temperatures. At room temperature there is reasonable agreement between different methods, but at low temperatures such meagre X-ray data as exist suggest that the apparent Θ values may be lower than those found by other methods. It would seem that some accurate and comprehensive X-ray work in this field would be rewarding.

Two papers were given on the contribution of nuclear magnetic resonance to studying thermal motion. In a review of this application, Prof. E. R. Andrew emphasized that whereas previous speakers had been concerned solely with 'vibrations', there were other forms of motion, such as hindered rotation and self-diffusion, which only occurred infrequently—though involving much greater movements—and which could not be examined by diffraction techniques. Examples were given of how these topics can be investigated quantitatively by nuclear magnetic resonance techniques and how the postulated effects on the spectrum can also be demonstrated by absorption measurements with rotating crystals. Dr. J. A. S. Smith described an application of nuclear magnetic resonance methods to the examination of single crystals of urea and thiourea which demonstrated the onset of hindered rotation about the C=O and C=S bonds in the two cases. As a result the molecules flip between two possible equilibrium configurations, giving rise to large apparent temperature factors for some of the atoms as judged by X-ray diffraction work.

In conclusion, it may be worth recording two personal impressions which remain from the papers and discussions. First, although the precision of experimental measurements in these investigations is very high, there still remain some significant gaps in interpretation which leave room for systematic errors and may make some of the apparent accuracy illusory. Secondly, in spite of the increasing identity of equipment used over the world, one can still be struck by the individuality of thought and methods of approach which characterizes the different schools of investigators.

The symposium was attended by about 400 persons, mainly accommodated in the large lecture theatre of the Arts School at Cambridge, but with an over-flow in the adjoining Cavendish Laboratory served by a closed-circuit television set. It was perhaps significant that even for the less-crowded sessions there were many who preferred the quieter, airy contemplation of the television screen to the hurly-burly of the lecture room.

G. E. Bacon

THE INTERNATIONAL SCIENTIFIC FILM ASSOCIATION

THE fourteenth annual congress of the International Scientific Film Association was held in Prague during September 16–24. It was attended by 120 delegates and observers from twenty-four countries. The British delegation of twenty people was led by Mr. Edgar Anstey, president of the Scientific Film Association. Associated with the congress was the Third Festival of Films presenting Science.

The International Scientific Film Association is a non-profit-making and non-governmental organization, officially recognized for consultative status with Unesco. Membership is open to any organization representative of the science film movement in the country of that organization.

The congress were welcomed officially by the Czechoslovak Minister of Education and Culture, Dr. Frantisek Kahuda, and by the managing director of Czechoslovak Film, Mr. Alois Polednak.

The Czech Organizing Committee—led by Dr. Vladimir Vaclavek—provided a delightful centre in

the form of the Film Club, at which members of the congress could meet and also dine and drink until the early hours of the morning. They also provided facilities for many visits in their beautiful city of Prague, and opportunities for meeting film makers and scientists in their studios and laboratories. The social life was full and active.

The first International Library for Scientific Film is to be set up in Brussels. It is the result of an agreement between the International Scientific Film Association and the Belgian Institut National du Cinéma Scientifique. There has been much discussion over this film library, and the stage has now been reached where the final documents are likely to be signed sometime in 1961. Van den Borre, director-general of the Belgian Ministry of Education, expressed to the general assembly his Government's keen determination to see the project through, and gave some details of financial support. The main tasks of the Library will be to gather together and keep copies of the best scientific films, to classify them, to publish general and specialized catalogues, to organize congresses, and to arrange special showings of films.

Because cinema and television are rapidly becoming closely linked, resulting in many new problems and possibilities for scientific film makers and users, it was agreed to set up a commission to study television in relation to the aims of the scientific film.

Unesco has suggested a study be made on the provision of films in the natural sciences for use in high-schools in newly developing countries. The International Scientific Film Association has been asked to undertake the research, and a commission was set up for this.

Closer co-operation between the Association and specialized international bodies and associations having film sections, for example, the World Veterinary Association, is to be secured by making provision for observers from these bodies to attend Association's congresses.

Greece and Israel were admitted to full membership of the Association, bringing the number of member countries to twenty-eight. It is expected that next year the American Science Film Association is likely to become a member.

The annual congress provides the main discussion opportunity for international science film makers. To meet their needs, there are three sections, each having its own programme of work. They engage in a vast range of activities.

In the Research Section, 11 lectures and 35 reports were delivered, and 68 specialized films were shown. In the Education Section, 4 lectures and 24 reports were made and 62 films were shown. In the Popular Science Section, there was a major discussion on definition of popular science films, two reports were made, and 72 films were shown. In addition, the Popular Science Section organized for the first time three special meetings of television workers from different countries at which ten TV films were shown.

Two B.B.C. producers—Aubrey Singer and James McCloy—presented a clear picture of what was being done in B.B.C. television, and the B.B.C. won much praise for its co-operation in making available a large amount of TV recording.

The question of definition has very much bogged down discussion in the past, and for the first time this year it was felt that the beginning of a successful solution to this problem had been made. In the Popular Science Section, a paper entitled "Types and Genres of Popular Science Films" was read by Mr. Igor Vassilkov (U.S.S.R.). He divided popular science films into two groups—the didactic and the imaginative—and then used the terminology of literature, because the film has as yet developed no comparable language, to describe the different kinds of films to be found within each category. It was agreed that the nature of such a film is determined by what the writer and director have set out to do. There was long discussion on this paper, in which the writer of this report found general acceptance for his view that the didactic film was now being taken over by TV and specially-made educational films, and that the future for the popular science film lay with the imaginative type of film. It was no longer necessary to popularize science among young people, but to stir their imagination with an understanding of the social implications of scientific development. It was mainly an older generation who had not been taught science at school, who still required the didactic type of popular science film.

The Popular Science Section has agreed to ask member countries to provide details of all the films already made or which will have been finished before January 1, 1961, concerned with the history of science and technology, or of the lives of eminent personalities in science and technology whose discoveries and inventions are of international significance. It will form the basis for a comprehensive catalogue to be published by the Russian branch of the Association.

Among problems that concerned the Education Section was the role of the film in speeding up the rate of learning, that is, to increase the amount learned without increasing the time spent in school. Mr. Vitali Jemtchujni (U.S.S.R.) gave details of a series of new teaching films in physics which were being prepared for production in his country and which were part of an overall attempt to find a solution to this urgent problem.

The Research Section considered films in medicine, biology and botany. Two Russian papers that aroused particular interest were on new Soviet equipment for high-speed still photography and cinematography, and the use of high-speed and ultra-speed filming of technological processes pertaining to agricultural machinery. The latter work has risen from problems caused by the mechanization of cotton harvesting. Film was used to obtain a picture of what happens in separating cotton lobes from the boles when cotton is picked with pneumatic harvesters. It was claimed that economies in picking and an increase of production resulted from the application of these studies.

The general assembly agreed to award diplomas to the following films shown during the Festival: "The Mountain Canal" (China); "Passsport to Space" (Czechoslovakia); "Sea Dancers" (France); "The Magic Tape" (German Federal Republic); "Living Traps" (Hungary); "Morning Sun" (Japan); "Sources of Energy in the Blood Circulatory System" (Poland); "The Revealing Eye" (Great Britain); and "Atomic Ice-Breaker" (U.S.S.R.).

In addition, "Symphony in Steel" (Japan) was given a special commendation for its use of cinemascope, as was "Timber" (Bulgaria) for its witty treatment of a static subject.

Mr. Alexandre Zgouridi (U.S.S.R.) was re-elected president of Association, and the vice-presidents are Mr. Edgar Anstey (Great Britain) and Mr. J. Varossieau (The Netherlands); the honorary secretary remains Mr. John Maddison, one of the founders of the Association, who this year wished to resign, but

was persuaded to stay on for another term. Mr. Mohamed Afifi (Morocco) was appointed assistant to the honorary secretary. The honorary treasurer is Dr. Vladimir Vaclavek (Czechoslovakia). The honorary life members remain M. Jean Painlevé (France) and Mr. Jan Korngold (Poland). The editor-in-chief of *Scientific Film*, the journal of the Association, is Mr. Maurice Goldsmith (Great Britain).

The liaison officer of the Association with the International Science Film Library is Mr. Luc Haesaerts (Belgium); the chairman of the Television Study Commission is Mr. John Maddison, and of the Unesco–International Scientific Film Association Science Films Commission, Mr. Bernard Chibnall (Great Britain). The chairmen of the Standing Committees are: Research, Dr. R. Robineaux (France); Popular Science, Mr. V. Tosi (Italy); and Education, Prof. J. Jacoby (Poland). Next year's Congress is likely to be held in Rabat, Morocco.

MAURICE GOLDSMITH

A BRITISH SOURCE OF NATURAL GAS

THAT in Britain there should be in daily use a supply of natural gas may well surprise many well-informed people. Indeed, it was in 1938 that two discoveries of natural gas in Britain were made, one at Cousland, south-east of Edinburgh, and the other west of Whitby at Eskdale. At that time no commercial outlet existed for these potential supplies and the wells were sealed off for eventual future use. The Cousland discovery has been harnessed by the Scottish Gas Board for the use of Musselburgh, where after being suitably treated it forms part of the gas supply.

Now there comes the news of interest more particularly to the inhabitants of the Whitby district of the actual utilization of the gas from the Eskdale area. The wells are situated in moorland of much natural beauty; but there is no fear that the amenities of that fair land will be impaired by the small surface equipment that marks the source of a sufficient supply of gas to serve a new but sole production unit in the Whitby Gas Works.

Two wells, of some eleven that have been drilled, have proved to be gas producers. These wells have a closed pressure approximating to 2,000 lb. per sq. in., and draw their gas from limestone layers, respectively 4,196 and 4,807 ft. below ground-level. It was only in April this year that these wells were re-opened and now the laying of a 3-in. pipe-line has been completed. Further, in order to produce from the natural gas, which contains 93–94 per cent of methane and has a calorific value of 1,000 B.T.U. per cu. ft., a final gas for public distribution of 500 B.T.U. per cu. ft., a conversion plant has also been installed.

The conversion process of the gas is known as a reforming process. It consists essentially of the reaction of the natural gas with steam to produce hydrogen and carbon monoxide. It is carried out in special heat-resisting steel tubes which are heated to about 1,100° C. and contain a nickel catalyst. It is then enriched with some cold natural gas, and flue gas from the tube-furnace, fired by natural gas. This is necessary to adjust it to the correct calorific value and density for public distribution.

It is also interesting to note that the gas is of such a freedom from sulphur impurity that in order to ensure that gas supplied to the town should have a distinct odour, equipment for the purpose has been installed, employing tetrahydrothiophen as odorant.

The two wells available have a combined flow-rate up to 4·5 m. cu. ft. per day. Three reformer units have been provided, each having a daily capacity of 625,000 cu. ft.

The plant has been put to work in recent weeks, and the venture is so new that the performance tests have yet to be carried out.

R. J. SARJANT

THE LIBRARY IN SCIENCE AND TECHNOLOGY

OF the papers of scientific interest presented at the annual conference of the Library Association at Scarborough, September 12–16, that of Dr. D. J. Urquhart describing the planning of the National Lending Library for Science and Technology and the ideas and motives behind it is undoubtedly the most important, but some of the other papers should not be overlooked by the scientist and technologist. In his presidential address on September 13, Mr. B. S. Page, librarian of the Brotherton Library, University of Leeds, discussed librarianship as he saw it practised in English universities of the twentieth century, and more particularly the research side of such work. Research, he suggested, in fact determined the extent, and very largely the character, of the collections and greatly influenced every aspect of the work of a university librarian, and Mr. Page emphasized, first, that the librarian and his readers were members of the same university community, with all it implied, and secondly, that the reader regarded the library less as an amenity than as a necessity; his use of it was regular and professional; normally his work could not proceed without it, and how it operated made an immense difference to the reader's peace of mind and perhaps his hopes for the future. From this Mr. Page argued that because selection had to make the most of very limited resources, buying must be largely related to specific interests which have to be known and understood by the library staff, while at the same time important works had to be acquired for future needs and a close watch kept over special collections and special emphases in general collections. The librarian must be thoroughly equipped to make the most of the potential co-operation of the experts in the teaching departments surrounding him and, pointing out that a university

library is being assembled for generations of scholars, Mr. Page claimed that the quality of library development could do much to make or mar the future welfare and importance of the university.

Mr. Page again emphasized the importance of the personal qualities of the librarian in referring to problems of cataloguing and classification, urging that the schemes to be adopted should not be such as to cause irritation or hindrance to the reader, and, besides putting in a word for the value of browsing among the open shelves as a source of inspiration and insight, he pleaded for imagination as well as knowledge on the part of the librarian and his staff. Techniques, he insisted, were means to an end and the librarian must be prepared to meet his readers on their own ground and to speak their language. Moreover, besides professional techniques, he needed specialized knowledge, experience of research, and the enthusiasm which came of such specialization. The ideals of personal acquaintance with books, personal help to readers, and unselfish devotion to the advancement of knowledge were as valid as when Henry Bradshaw formulated them in 1882.

Mr. M. C. Pottinger's account of libraries in the Soviet Union was of general rather than scientific interest. He commented on the generous provision of reading or study rooms as a common feature of Russian Libraries, and on the claim of the Bibliographical Reference Department, with a staff of about 100, at the Lenin State Library, Moscow, to supply bibliographies on any topic. In a subsequent paper to the conference, Mr. R. G. Surridge referred to the lack of attention to bibliography in libraries in Britain and suggested that a new well-designed Chaucer House, in co-operation with the National Central Library, should provide a comprehensive Bibliographical Department.

Miss L. V. Paulin's paper on "Technical Library Services" described some of the co-operative schemes that had been set up in Manchester, Sheffield, Liverpool and elsewhere in a field where any general co-ordinated policy was completely lacking. Most of the schemes, however, were for large cities where many highly developed libraries were already available and the greatest need was in the counties. The rapid development of adequate libraries in technical colleges provided an opportunity for remedying this position, and Miss Paulin quoted from the Ministry of Education's report on Technical Education of 1956 to indicate the opportunity that existed to build up a really integrated technical library service between the public library and the technical college. The most rural county to tackle the problem so far was Herefordshire, where a County Technical Library service, based on the Herefordshire Technical College, would begin in January 1961, but Northumberland and Durham were already co-operating with a Newcastle scheme, and Middlesex with a West London scheme. The Northamptonshire County Technical Library Service, started in July 1957 and based at Corby Technical College, was already experiencing a large potential demand, while in Hertfordshire a technical library and information service was based on technical colleges and completely integrated with the County Library. This pilot scheme was described in some detail by Miss Paulin, who stressed that such services in the country as a whole must be based on co-operation. The main requirements were receptiveness of mind among members of industrial and commercial firms and an awareness of the value of up-to-date information; a comprehensive, easily accessible collection of books, pamphlets and periodicals in the care of knowledgeable librarians, with the occasional assistance of technologists in dealing with inquiries; and equipment for documentary reproduction.

A following paper, by Dr. H. Coblans, on "International and Local Information", attempted to assess the present structure and likely trends of scientific and technical information services from a survey of a few characteristic countries, such as Switzerland, West Germany, France and Poland. On the international plane there were now signs of a more generous policy towards co-operation, and the International Atomic Energy Agency has created a Division of Scientific and Technical Information which publishes a number of bibliographical tools to implement the Agency's statutory responsibility to further the exchange of information among its member States. Urging caution as to the value of some of the new technical possibilities for transmission of information, such as 'Telex', which admittedly if imaginatively used could transform the effectiveness of information services, Dr. Coblans said that each country should endow and maintain a National Science Library adequately staffed to provide the rapid service that new techniques permit, while international governmental organizations must place their great resources of information fully at the disposal of the national centres. The technical advances, however, involved the obligation to re-think and re-shape some of the British principles of publication, bibliography, abstracting, copying and copyright and inter-library loan. Ultimately this should be done by international discussion and agreement, but national associations, such as the Library Association and the Association of Special Libraries and Information Bureaux, must take the first step.

Dr. Urquhart said that the site of 60 acres at Boston Spa, where it was hoped the first buildings of the new National Lending Library for Science and Technology would be ready at the end of this year, allowed for considerable elasticity in planning, and the present aim was to provide the practitioner in science or technology with all the current literature of the world he might need. They were only trying to obtain the older literature where they had evidence of demand, or where it did not exist in a readily accessible collection, but they were prepared to accept and make available scientific and technological literature of any age. The Library should become fully operational in September 1962, and only then could the extent to which it would be able to meet the demand on its services be measured; at present, however, its collection could provide about 90 per cent of the Russian literature and translation which are requested. Staff was being selected so that collectively it could understand not only the language of science but also the increasing number of national languages in which science was written. It was hoped to transfer the 1,000 tons of literature from London to Yorkshire without closing any service, and although it was expected that some requests would go to the Science Museum Library which should have been sent to Boston Spa, the handling of such requests would be simplified by use of the same type of forms.

Dr. Urquhart said it was not intended to start any large technical information service, but rather to

assist existing services where possible by directing attention to any literature in their fields of which they might otherwise be unaware, though it would be part of the new Library's responsibility to see that attention was given to any gaps in the technical information services which might develop: one such gap had emerged with regard to Russian translations, on which the Library was now spending more than £100,000. Dealing more particularly with the relations of the new Library to the rest of the library system, Dr. Urquhart said that in the near future some of the larger libraries and the special libraries would be invited to notify the Library systematically about new serials or conference proceedings which they decided not to acquire, but for which they might have some future need. On the collecting side they would invite all libraries to let them know of publications in the National Library's field for which they received an embarrassing volume of requests for inter-library loans. By collecting such material the new Library would help the inter-library loan arrangements to work more smoothly, but at present the potential loan demand on the new Library seemed to be increasing, and Dr. Urquhart thought the tendency was likely to continue, particularly because the new Library's loan service would be faster than the existing services. Accordingly, they were very interested in efforts to tune up the inter-library loan system. He thought there was no fundamental reason to prevent evolution of a national inter-library loan form using the prepaid flat-rate system for postage.

Irrespective of its effect on inter-library loan procedure, the existence of the National Lending Library for Science and Technology might well have more profound effects, such as producing a demand for a national lending library for the humanities, possibly based on the National Central Library. Dr. Urquhart, however, left this for future consideration and referred them to the relations of the new Library with local libraries, emphasizing that the potentialities of the comprehensive collection of scientific literature at Boston Spa could not be fully utilized unless the potential users in each locality could discover what they wanted to read, that is, unless guides to the literature of science were available locally. We needed a form of co-operation in which local libraries would assist potential users to find out what they wanted to read, and the National Lending Library would, if necessary, supply this literature. It was intended that such co-operation would be based on the idea that each partner in the scheme would pay his own expenses, and they had recently written about this idea to every local authority and technical college in the United Kingdom. At present, however, standards of technical library service available to the public in many areas were not high: a standard which technologists might criticize as inadequate was attained by only eighteen public libraries and seventeen technical college libraries, and in consequence the National Library was building up some sets of bibliographical tools to lend to libraries which are considering developing their bibliographical collections. They had also been thinking about relations with the public libraries and about the training of librarians, and in conclusion Dr. Urquhart urged that future policy must be based on the scientific analysis of the facts.

CHEMICAL DOCUMENTATION

CHEMISTS nowadays are increasingly eager to receive new chemical matter "hot from the press" but many find it impossible to cope quickly with the mass of information contained in the many traditional journals appearing almost hourly. A few years ago the Chemical Society made a great effort to save the chemist's time by introducing a monthly publication, *Current Chemical Papers*, in which some hundreds of selected titles of papers taken from more than four hundred chemical journals of note were set down under their appropriate sections. The undoubted success of *Current Chemical Papers* has led the American Chemical Society to copy the essentials of the scheme with the publication on an experimental basis of *Chemical Titles**.

The major difference is that *Chemical Titles* is produced by machines and thus may claim a potential wider coverage and give greater detail.

The titles of some five hundred journals, translated where necessary, are punched on to I.B.M. cards together with the authors' names and journal references and are then fed to computers. Within two hours the new journal appears containing three parts. The first part consists of a permuted title index in which key-words from each title have been arranged alphabetically down the centre line of the column. The second part consists of an alphabetical list of first listed authors together with the titles of their current papers published in the selected journals. The third part (in No. 2 only) gives an index of authors other than the first listed for each paper along with the code reference for the paper.

In addition to the key-word, each horizontal line contains as much of the remainder of the title as the machine's programme permits and thus assists in selection of significant titles.

The system is used by scanning vertically the alphabetical key-word list and then, when interest is seized, by reading the horizontal text. When more information is required the reference code on the right-hand side of the entry is noted and located in the alphabetical author index.

The whole system of making the reference code, etc., and for using the system are described fully in the introduction. It is a very clever and easily understood system which appears to work.

The contents of some 550 journals have been dealt with, and it is planned to make a semi-monthly issue of 2,000–3,000 titles.

A good many improvements have been made in No. 2, especially in editing, and more will be made as experiments proceed and as suggestions and criticisms are received. The printing will need to be much better and larger if possible.

The publication fully justifies the claim that it increases "current awareness". It will probably be of

* *Chemical Titles*. No. 1, April 1960, 101 pp.; No. 2, May 1960, 89 pp. Chem. Abs. Service. American Chemical Society

particular value to the industrial chemist anxious to keep "right up to date on the literature".

The course of such an experimental system will be watched with great interest. Its eventual success may well depend on the cost of its production and it remains to be seen whether American machines directed by Malcolm Dyson can do a cheaper and more useful job for chemical documentation than is being done at present by the carefully selective man- and woman-power behind *Current Chemical Papers*. M. Stacey

MEASUREMENT AND CONTROL OF MOIRÉ FRINGES

THE illustrated booklet "Moiré Fringes for Measurement and Control", prepared by the National Physical Laboratory and the National Engineering Laboratory for members of the machine-tool and engineering industries, gives a brief account of the essential features of moiré-fringe methods and some of their engineering applications (Pp. 11. London: Department of Scientific and Industrial Research, 1960).

Moiré fringes are the pattern of relatively broad equidistant bands produced when two gratings with equal-line spacings are placed face to face, but with the sets of lines not quite parallel to each other. When one of the gratings is moved in the direction at right angles to the lines on it, the fringes move through exactly one fringe spacing as the fringe moves through one grating-line spacing. The variation in brightness as the fringe moves can be detected by a photoelectric cell and the linear movement can therefore be converted into a corresponding electrical signal. Gratings can be produced with radial lines also and thus angular movement can be measured or recorded electrically. Methods for the production of gratings at a reasonable price in the quantities and sizes for industrial use have recently been developed, and copies of master gratings produced at the National Physical Laboratory and National Engineering Laboratory are now available commercially. For most engineering applications gratings with about 1,000 lines per inch are required, but gratings up to 10 in. long with up to 10,000 lines per inch or even glass gratings up to 3 ft. long for special purposes can be produced.

Since moiré fringes are produced by very many accurately spaced grating lines and the effect of any errors of spacing of individual lines is reduced by the averaging process which occurs in the production of fringes, great accuracy in measurement is obtainable by using the fringes. Both analogue and digital systems can be used to handle the photoelectric signals, and various applications related to the automatic positioning of machine tools are described in the booklet. It is emphasized that the successful use of moiré-fringe systems requires specialized optical and electronic techniques and that to obtain maximum advantage from the use of moiré fringes in the machine tool field, close co-operation is required between the mechanical engineer and optical and electronic experts. Future developments of the application of the moiré-fringe technique may revolutionize the design of machine tools and the accuracy of their products.

The secondment of members of the staffs of industrial firms to the National Physical Laboratory and National Engineering Laboratory would be a particularly valuable way of speeding up progress, and the laboratories extend, in the booklet, an invitation to firms with electronic, optical or engineering interests to work with them on projects of mutual interest.

GRAFT VERSUS HOST REACTIONS ON THE CHORIOALLANTOIC MEMBRANE OF THE CHICK EMBRYO

By Sir MACFARLANE BURNET, O.M., F.R.S., and DEBORAH BURNET

Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia

THE clonal selection theory of immunity[1] in its present form postulates that in the normal animal a large proportion (perhaps all) of the mesenchymal cells could be divided into clones, each of which is pre-adapted to react with one or other of two antigenic determinant patterns. (The alternatives of being able to react with one, three or four such determinants have not yet been excluded.) The initial distribution of these reactivities is essentially at random, and in the present context there is no call to discuss how the patterns have arisen or how this random distribution to the ancestors of the marked clones could be accomplished. By hypothesis, in the adult there are no clones which can react with normal accessible components of the individual concerned, but there are present clones representing all types of antigenic determinant not present in the body.

Antibody production is presumed to occur in two phases corresponding (1) to the inductive phase and (2) to the productive phase of orthodox immunological theory. In the inductive phase two processes occur: there is proliferation of the clone to produce many more members and the newly produced cells have an increased reactivity with the corresponding antigenic determinant. In the second phase, renewed contact with the antigenic determinant results in proliferation, conversion to the plasma cell form and production of antibody.

According to orthodox immunological theory (for example, ref. 2), the interpretation of the secondary productive phase is not significantly different

from one based on clonal selection. For quantitative experiments on antibody production, it is almost obligatory to use the secondary phase simply in order to have an adequate concentration of antibody. No possibility, therefore, exists of differentiating directly between the two theories by any experiments in which serum antibody is measured.

For the inductive phase, we have two very different conceptions. On the 'instructive' Landsteiner–Pauling theory the period is occupied by the entry of antigen into macrophages, its conversion into a template form and its transfer to plasma cells in one form or another. On the clonal selection theory the inductive period represents the time needed for stimulated cells of pre-existent clones to multiply to a detectable level and in the process increase their reactivity so as to respond by antibody production to a new stimulus.

To differentiate between the two theories we need to find a technique by which it can be shown that a given population of normal lymphoid cells is either: (*a*) uniform or nearly so in its immunological potentialities, or (*b*) contains a minute proportion of cells differentiable from the rest by their ability to react with a definable antigen.

One could establish an 'instructive' theory by showing that, no matter how small the number of lymphoid cells taken, antibody could be produced or some other definable immunological competence demonstrated against a range of antigens.

To establish a selective theory, we need the equivalent of a plating method. If we are looking for a mutant (or a contaminant) present in a bacterial culture in a proportion of 10^{-4}, the only way to detect it is to plate the culture on some medium so chosen that the normal form gives no evidence of its existence while the mutant or contaminant discloses its presence by forming a colony. Colony counts on a series of normal and differential media will allow a quantitative analysis of the different clones in any bacterial culture.

In the method we have devised for studying the Simonsen phenomenon[3] on the chorioallantoic membrane[4,5], we have something closely resembling a plating method. Briefly, blood or separated leucocytes from a normal fowl is inoculated in 0·1 ml. amount corresponding to about 5×10^5 leucocytes on to the dropped chorioallantoic membranes of 12-day chick embryos. When examined four days later, discrete focal lesions, in number usually between 10 and 100, and with a general resemblance to viral lesions such as those produced by herpes simplex, are observed.

Our own experience is in line with Terasaki's[6] finding that the cells responsible for the Simonsen phenomenon judged by splenic enlargement after intravenous inoculation are lymphocytes. His estimate that the minimum effective dose is of the order of 10^4 lymphocytes also agrees with our estimate of 2×10^4 leucocytes per chorioallantoic focus.

To be effective leucocytes must be from an immunologically mature bird; embryonic blood or spleen is inert. Further, when the donor of leucocytes and test embryos are from the same pure line, a high proportion of membranes show no foci. By analogy with a wide variety of similar quantitative methods, it can be assumed that each focus is induced by a single cell and that basically it is initiated by an immunologically competent cell which either possesses or can acquire specific reactivity against a foreign antigenic determinant in the chick embryo.

Table 1. Titration Results used for Figs. 1 and 2

Donor	Foci on substrain (1) membranes	Adjustment
4318 1*	0 0 0 0 0	—
2*	3 2 1 1 1 0 0 0 0 0 0	× 2
3763 1	*57 33* 5 4 4 1 1 1 0	× 1·1
2	120 100 *90 86 85 82 78 75 75* 57 52 40 34 20 15 10 3 1 1 1 1 0 0	× 0·62
3	*34 34 33 31 30* 20 15 8 7 7 1 0 0 0 0 0	× 1·5

* Counts on random membranes inoculated in parallel included 4318 (1) 40 35 30 19 (2) 36 35 26 22

Through the co-operation of Dr. J. M. Rendell and Dr. J. A. Morris, we have had an opportunity of using two relatively pure-line stocks of White Leghorns maintained at the Werribee Poultry Research Section of the Commonwealth Scientific and Industrial Research Organization. Most of the experimental work in 1959–60 was done with substrains (1) and (2) of their *B*1 line. As many workers have found, pure-line eggs tend to show a low proportion of fully viable embryos, and we have had to deal with smaller groups than we would like; but the trend of results has been quite consistent.

From a preliminary survey of results when cells from the present fowls were tested on embryos of the same group, it was clear that a large proportion of membranes showed zero or very low counts from inocula producing normal numbers of foci on unrelated embryos. Two birds of group (1), the cock 4318 used for fertilization (by artificial insemination) of the whole group and one of the hens 3763, were chosen for more detailed examination. The results are shown in Table 1. It is clear that the pattern of counts differs, 4318 producing few or no foci on all membranes, while 3763 in each experiment gave a conspicuous group of high counts as well as a large number of zero or very low counts. In order to allow consolidation of the whole series in one figure, the three experiments with 3763 were brought into conformity by taking the level of the 'high sequence' as 45, 80 and 33 respectively, and adjusting this to 50 by multiplying each observed count by the appropriate factor (1·1, 0·62, 1·5).

In the graphs, each adjusted value is shown as a dot and the distribution indicated by the use of a moving aggregate covering five digits on either side of each unit on the abscissae. Ordinates therefore represent the number of embryos showing counts over the range $\pm$ of the value indicated.

In order to provide a model against which the observed distributions can be compared, we have made the preliminary assumption that in our 'pure line' stock (1) we are dealing with two unlinked loci each with three possible alleles ABC and DEF and that antigens ABCDEF are directly related to the corresponding genes. There are probably many other genetic models which could replace this one but it is preferred merely as being simple to handle. By the clonal selection theory each bird will have lymphocytes of those patterns among a, b, c, d, e, f, which correspond to the antigens not present in its cells. If we have a bird of genetic constitution AA/DD, its relevant clones will be of patterns *b*, *c*, *e* and *f*, while AB/DE will have only *c* and *f*. We assume that our flock has come to approach the degree of homozygosity indicated by AA/DD so that although all genes are present the combinations AA and DD are four times and AB and DE twice as frequent as any of the others. If a sire AB/DE covers a flock of such composition one can deduce the distribution of

genotypes among the embryos from eggs he has fertilized. We can also assume that in any given blood sample the proportion of cells in the allowable clones will have some characteristic value not necessarily the same for each clone. By a process of trial and error to find conditions that will fit the observations, we have arbitrarily assigned to our two 'pure-line' donors cock 4318 and hen 3763, the constitutions shown in Table 2. The sort of counts of foci that would be obtained by this hypothesis on embryos sired by 4318 from a flock of the type postulated can be seen from Table 3. On a random set of embryos produced under the conditions mentioned earlier, one can readily calculate the distribution to be expected with these two sets of leucocytes.

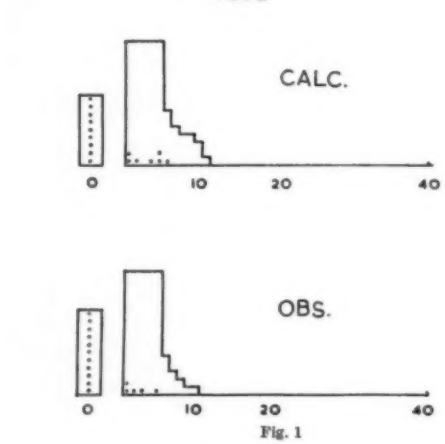

Fig. 1

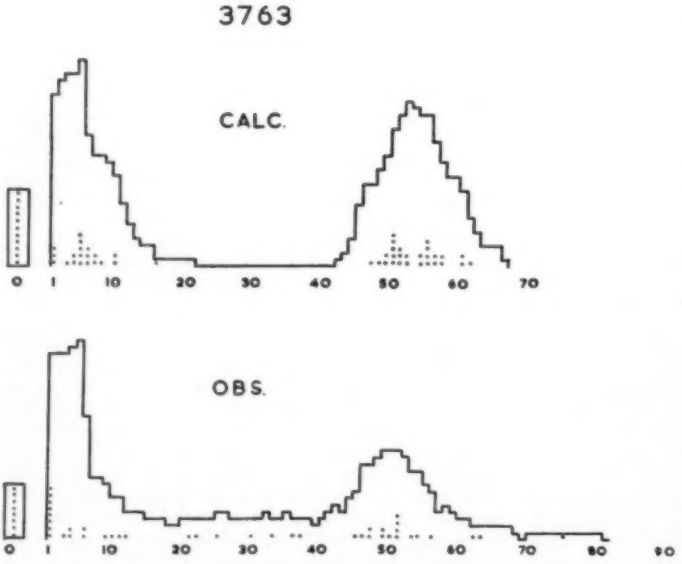

Fig. 2

Figs. 1 and 2. Distribution of focal counts when leucocytes from birds shown—4318 (*m*) and 3763 (*f*)—were tested on chorioallantoic membranes of the same pure line. Each dot represents one count of the value shown by the abscissæ and the line is a moving aggregate to include the number of counts within the range ± 5 of each value. Calc.: the results expected from the assumptions described in the text

Table 2. Hypothetical Constitution of Donors of Leucocytes

Bird	Genotype	Antigens	Clones and number of cells per 0·1 ml.
4318	AB/DE	ABDE	*c*(5) *f*(1)
3763	AA/DD	AD	*b*(50) *c*(5) *e*(5) *f*(1)

Table 3. Calculated Counts of Foci on Different Embryo Genotypes

Embryo genotype	Counts from standard inocula from	
	3763 AA/DD	4318 AB/DE
AA/DD	0	0
AA/DE	5	0
AB/DE	55	0
AB/EF	56	1
BC/EF	61	6

These calculated distributions are compared directly with those observed experimentally in Figs. 1 and 2, which show that by appropriate assumptions it is possible to obtain an excellent agreement between observed and calculated results. The agreement itself is unimportant but the general character of the experimental distribution is unmistakable and significant.

With completion of the laying period of the fowls used in the 1959–60 studies, the birds were divided into pairs and reciprocal skin grafts made. These tests made in collaboration with Dr. J. K. Dineen involved 20 double tests. The overall results were: 6 (15 per cent) rapid rejection, 25 (62·5 per cent) slow rejection and 9 (22·5 per cent) prolonged survival beyond 30 days. This is in accord with the degree of heterozygosis to be expected from the results of the chorioallantoic membrane tests.

The findings so far discussed were made in season 1959–60. With the availability of new-season birds of the next generation, we have now been able to obtain similar patterns of segregation, in groups descended from both substrains (1) and (2) of 1959–60. In one set of tests an unusually large set of eggs of group (2) allowed the use of several embryos of identical parentage. The embryos were all sired by cock 106 on seven of his full sisters, and were tested with leucocytes of the sire and of one of the hens 4442. The results are shown in Table 4. Other tests have shown that patterns similar to those obtained with substrain (1) (3763 and 4318) can be obtained with birds and embryos of the same substrain of the 1960–61 stock. Again as in the previous year when substrain (2) leucocytes are tested on substrain (1) embryos, there is no significant reduction in focal count below that obtained on random embryos. In expressing the results in provisional genetic form, different symbols must therefore be used for the two substrains.

For substrain (2), the symbols PQR may be used for the genes and antigens concerned. If we neglect all low counts, the results in Table 4 can be expressed in terms of 2

Table 4. RESULTS OF TESTS ON INBRED LINE (2), 1960–61 SEASON

Leucocyte donor	Tested on embryos	Focal counts	Random control: median count
106 (M)	683 × 106	1, 1, 1, 0, 0	52
,,	4385 × 106	4, 2, 1	
,,	4525 × 106	**150, 123**, 0, 0	
4326 (F)	276 × 106	**65**	70
,,	4326 × 106	5, 5, 2, 1, 0	
,,	4525 × 106	0	

alleles only—birds 106, 683, 4326 and 4385 can be classed as PP with leucocytes of reactivity *q*, 4525 being PQ and 276 PQ or QQ. Obviously minor interactions also take place, but these need not be elaborated on here.

These finding are in accord with what would be predicted on three assumptions: (*a*) that preadapted immunologically competent cells, presumably lymphocytes, are present in normal fowl blood and that the immunological patterns they carry correspond to antigenic determinants not present in the donor; (*b*) that the focal lesions are initiated by an immunological reaction; (*c*) that tissue antigens in chickens are genetically controlled. Since no immunologist is likely to dispute (*b*) and (*c*), the results can be claimed as providing at least *prima facie* support for the clonal selection theory.

If one seeks to interpret the present findings on any other general hypothesis of immunity or antibody formation, the following points seem to be relevant: (1) The histological development of foci suggests strongly that the effective cell initiates the focus, presumably by starting to multiply, within a few hours of lodgment on the chorioallantois. 'Recognition' that the cell is in contact with a foreign antigen is therefore a rapid process. (2) Washed cells are effective so that Jerne's selection theory[7] cannot be invoked. (3) If the clonal selection theory is not accepted, each effective cell must carry all the necessary information to recognize the foreignness of its surroundings and then develop an immunological reactivity directed against the foreign element.

By appropriate *ad hoc* qualifications it would undoubtedly be possible to describe our findings in terms of an instructive hypothesis of the Landsteiner–Pauling type or of a selection theory by which each mesenchymal cell carried all potentialities of immunological reactivity. The advantage of the clonal selection hypothesis lies simply in the natural fashion with which it covers the results.

The most important points against the clonal view that we have been able to recognize in the present results are: (*a*) Allowing for a 'plating efficiency', which is probably below unity, the number of foci obtained when by hypothesis only one foreign antigenic determinant is present is sometimes higher than it seems reasonable to expect. (*b*) Just as many, or more, foci are produced when there can be only one foreign antigen as are obtained on random embryos where there should be several foreign antigenic determinants.

Both findings suggest that the number of cells capable of initiating lesions in response to the antigenic determinants involved is not determined wholly by random processes. We can reasonably hope that with progressive clarification of the immunogenetics of our system, it will become possible to examine in some detail the processes which determine focal counts and by implication the proportion of immunologically competent cells. Irrespective of theories of immunity, the special virtues of the chorioallantoic membrane system can scarcely fail to provide important opportunities to improve understanding of cellular immunology.

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DEVELOPMENT OF A SUB-LINE OF MOUSE SARCOMA-180 CAPABLE OF GROWING IN PYRIDOXINE-DEFICIENT ANIMALS

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THE occurrence of various adaptive processes in populations of neoplastic or bacterial cells is indicated by the tendency of such cells to increase their capacity for growth under adverse conditions. Changes in the growth capacity of neoplastic cells have been associated with the development *in vitro* and *in vivo* of tumour sub-lines resistant to treatment with antimetabolites. Several observations indicate that available antimetabolites of pyridoxine and folic acid do not always duplicate the effects of the nutritional deficiency of these vitamins[1–3]. In experiments described here, a nutritional depletion of an essential factor *in vivo* has been used, to our knowledge, for the first time as a selective pressure to alter the growth capacity of mammalian cells.

During work on the influence of vitamin deficiencies on experimental tumours in rodents, a high incidence of complete regression of mouse sarcoma 180 (*S*-180) following impairment of tumour growth was observed in Swiss mice which were fed a pyridoxine-deficient diet[4]. These observations provided a basis for attempting the selection of a sub-line of *S*-180 capable of growing in the deficient animals. The development of such a tumour was achieved following repeated transplantations in vitamin B_6-depleted mice.

Mammalian cells cultured in a semi-synthetic medium have a definite requirement for pyridoxine[5]. A similar requirement for the optimal growth of tumours may be indicated by the impaired growth of some induced and transplantable tumours in animals depleted of this vitamin[4,6–9]. Inhibition of growth and occasional regressions also occurred when, in addition to receiving the deficient diet, the tumour-bearing animals were treated with the pyridoxine

antagonist, 4-deoxypyridoxine[10–15]. Experiments were carried out in this laboratory on several transplantable tumours using dietary depletion alone to avoid any non-specific effect which may be associated with treatment with such antagonists. Marked retardation of neoplastic growth was observed in most cases; this effect, however, was transient. In some instances the sensitivity of different hosts to the vitamin deficiency did not permit a selective anti-tumour effect[16]. The impairment of *S*-180 in pyridoxine-deficient *HaICR* Swiss mice was striking, however, not only because the growth of the tumour was selectively inhibited, but also because 30–80 per cent of the implanted neoplasms regressed completely after initial growth[4]. Of several thousand compounds tested for activity against *S*-180, a limited number of these depressed the rate of growth of this tumour. Complete resorption of *S*-180 has been observed, however, only after treatment with 6-mercaptopurine and related purine analogues[17]. Thus, the regression of this tumour in pyridoxine-deficient animals is of particular interest.

The sub-line of *S*-180, designated *S*-180/B_6, was developed over a period of eight months by a gradual increase of the severity of vitamin depletion of the host mice. The standard procedures followed for the implantation of the tumours, the evaluation of tumour growth, and the preparation of the purified diets have been described previously[4]. Tumours were implanted into groups of 3–5 mice. In initial experiments *S*-180 was implanted in mice which were fed the pyridoxine-deficient diet beginning two weeks prior to implantation; this period of dietary depletion has been, in our experience, the minimum one which caused significant effects on the tumour[4]. These neoplasms, however, were invariably lost on two to three repeated transplantations into similarly depleted mice. Further attempts were successful when the period of depletion of the animals in which *S*-180 was to be implanted was prolonged gradually.

The growth of the tumour at different stages during the process of selection is indicated in Fig. 1 by the size of the tumours on the 8th day after implantation. In Fig. 2, progressive rate of growth of successive implants is shown. The sub-line was developed as follows. An 8-day-old *S*-180 tumour (8·3 mm.) grown in mice which were fed a complete diet was transferred

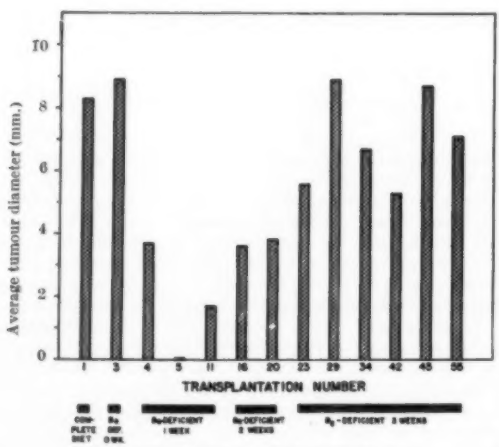

Fig. 1. Selection of a sub-line of *S*-180 capable of growing in pyridoxine-deficient mice

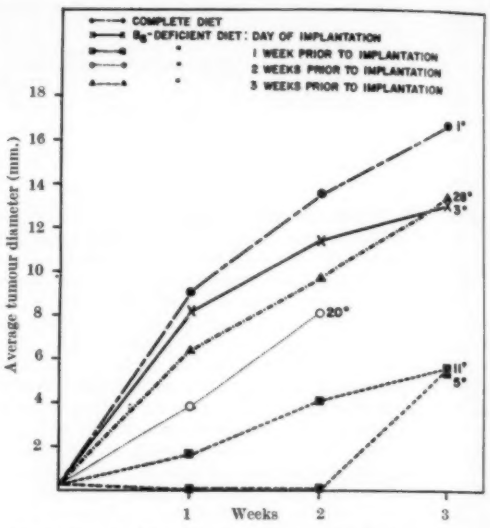

Fig. 2. Growth of *S*-180 during the course of successive implantations in pyridoxine-deficient mice

• Serial numbers of transplantation from the beginning of the experiment.

to mice fed the deficient diet from the day of implantation. On the 8th day of growth these tumours (7·8 mm.) were implanted in mice which were then fed the deficient diet (transplant No. 3). Eight days later the tumours (8·9 mm.) were implanted in mice fed the deficient diet starting one week prior to implantation. When these tumours were 8-days old (3·7 mm.) they were implanted again in similarly depleted mice (transplant No. 5). The tumour did not grow for 2 weeks (see Fig. 2); during the 3rd week 1 tumour out of 3 grew to a size of 5·4 mm., and this tumour was transferred to mice depleted of pyridoxine for 1 week before implantation. Following the next 5 successive transfers in similarly depleted mice, the tumour reached a size larger than 4·0 mm. in 2 weeks and was transplanted at the end of this period. Growth following transplant No. 11 is shown in Figs. 1 and 2. At this point the rate of growth of the tumour seemed well stabilized, and transplantations into mice fed the deficient diet for 2 weeks prior to implantation were begun. The rate of growth of the tumour increased gradually during the 9 subsequent passages (the size of the tumour was 4·2 mm. 2 weeks after transplant No. 12 and 8·1 mm. 2 weeks after transplant No. 20). From transplantation No. 21 on, the tumour was repeatedly implanted in mice which were fed the deficient diet for 3 weeks prior to implantation. At transplantation No. 23 and thereafter, the tumour reached a size larger than 5·0 mm. in 1 week and was always transplanted at the end of this period (growth following transplantation No. 28 is shown in Fig. 2). Growth was variable in subsequent transplantations (see Fig. 1), but in every instance the tumour, now called *S*-180/B_6, maintained its capacity to grow in the deficient mice. This tumour is currently carried in our laboratory in mice fed the pyridoxine-deficient diet beginning 3 weeks prior to implantation and is now in its 125th passage.

Simultaneous transplantations of *S*-180/B_6 into the right axilla and of *S*-180 into the left axilla of the same deficient or normal animals were performed at

Table 1. GROWTH OF *S*-180/B_6 AND *S*-180 IMPLANTED BILATERALLY IN THE SAME MICE FED A COMPLETE OR A PYRIDOXINE-DEFICIENT DIET*

Diet	8th day after implantation Av. tumour diam. ± *S.D.*		15th day after implantation Av. tumour diam. ± *S.D.*		Week preceding death† Av. tumour diam. ± *S.D.*		No. of regressions	
	S-180/B_6 mm.	*S*-180 mm.	*S*-180/B_6 mm.	*S*-180 mm.	*S*-180/B_6 mm.	*S*-180 mm.	*S*-180/B_6	*S*-180
Complete	8·3 ± 0·8	10·4 ± 1·4	11·5 ± 1·1	10·0 ± 2·0	9·7 ± 1·9	9·7 ± 1·1	0	0
Pyridoxine-deficient	7·7 ± 0·6	2·0 ± 0·6	11·8 ± 2·0	1·4 ± 2·1	15·4 ± 5·0	2·4 ± 3·1	0	5

* The purified diets were fed starting 3 weeks prior to implantation. Ten animals were used in each group. Transplant No. 28 of *S*-180/B_6 was used in this experiment.

† The figures shown were derived from the last measurements of the palpable tumours which were taken prior to the death of the animals. The mice fed the complete diet died as a consequence of tumour growth during the 2nd and 3rd week after implantation; those fed the deficient diet died during the 2nd to the 5th week after implantation.

the 28th passage of *S*-180/B_6 (Table 1). *S*-180 and *S*-180/B_6, implanted bilaterally in animals fed the complete diet, grew at a comparable rate. In contrast, when the two tumours were implanted simultaneously in the same pyridoxine-deficient mice, *S*-180/B_6 grew progressively whereas *S*-180 was greatly impaired and regressed in half of the animals. A similar test using 10–30 mice per group was performed at the 23rd, 41st, 57th, 72nd, 81st and 104th passage of *S*-180/B_6 with comparable results. Similar differences of growth were observed when the two tumours were implanted in separate mice fed complete or pyridoxine-deficient diets. This observation excluded the possibility of any interference of one tumour on the growth of the other when both of them were implanted bilaterally in the same mice.

The results reported above clearly indicate that *S*-180/B_6 is capable of growing progressively in deficient mice in which *S*-180 is greatly impaired. If this adaptation concerns an alteration in metabolism involving pyridoxine, the pertinent biochemical changes would be of particular interest. If, on the other hand, the selection *in vivo* involves the outgrowth of cells less influenced by host defence mechanisms, an opportunity is provided for the study of factors modifying the tumour–host relationship.

Following partial hepatectomy of pyridoxine-deficient rats, the content of vitamin B_6 in the regenerated liver was similar to that of the surgically excised portion of the same organ, suggesting that the vitamin might be transferred to the liver from other tissues[18]. Similarly, the adapted tumour might have greater capacity than the parent tumour to bind pyridoxine derivatives. Therefore, the vitamin B_6 content of the two tumours was measured. Both *S*-180 and *S*-180/B_6 tumours, grown in deficient hosts, had a similar low content of total vitamin B_6 (Table 2). The striking difference in rate of growth of the two tumours in the same deficient host, despite the similar vitamin content of the two tissues, infers that differences in the efficiency of enzymatic reactions related to growth might occur. Since such differences could be associated with the function of specific forms of the vitamin, experiments are in progress in collaboration with Dr. James A. Bain of Emory University to measure the content of pyridoxine, pyridoxal, pyridoxamine and their phosphorylated derivatives in *S*-180 and *S*-180/B_6.

Table 2. PYRIDOXINE CONTENT OF *S*-180/B_6 AND *S*-180 FROM ANIMALS FED COMPLETE AND PYRIDOXINE-DEFICIENT DIETS

Tumour	No. of assays*	Average content of pyridoxine ± *S.D.* Complete diet†	Pyridoxine-deficient diet†
		μgm. per gm. wet weight	
S-180	12	0·66 ± 0·16	0·17 ± 0·07
S-180/B_6	8	0·78 ± 0·24	0·14 ± 0·04
S-180‡	1	0·50	0·14
S-180/B_6‡	1	0·50	0·12

* For each assay, 5 to 20 tumours of each experimental group were pooled on the 8th day after implantation. The microbial assay (*Saccharomyces carlsbergensis*, ATCC No. 9080) measures the total content of the different forms of vitamin B_6 following acid hydrolysis of the samples. All values are related to pyridoxine as the free base.

† Diets were fed starting 3 weeks prior to implantation.

‡ Tumours were implanted bilaterally in the same animals.

Although the Swiss mouse is not genetically homogeneous and *S*-180 is not, therefore, truly compatible with this host, this tumour does not normally regress in these animals. Indeed, regressions were not observed even after treatment with compounds capable of depressing markedly the rate of growth of *S*-180[19,20]. As mentioned previously, regressions of this tumour in Swiss mice following chemotherapy were observed only in animals treated with certain purine analogues[17]. The observation that cortisone prevented the regressions of different tumours induced by 6-mercaptopurine suggested that this effect was partially dependent upon host factors[21]. The regression of *S*-180 in Swiss mice depleted of pyridoxine seems also partially dependent on host mechanisms directed against this tumour. Indeed, treatment of the depleted mice with cortisone[4], and total-body irradiation of the depleted animals prior to tumour implantation[22] markedly reduced the incidence of regression of *S*-180. That the Swiss mouse possesses potential defence mechanisms against *S*-180, which can become evident in certain experimental conditions, was suggested, also, by the regression of this tumour in mice treated with 'Zymosan'[23] or infected with BCG (Bacillus Calmette-Guérin) as long as two months prior to tumour implantation[24]. Although the nature of these defence mechanisms has not yet been clarified, the possibility exists that the regression of *S*-180 in Swiss mice depleted of pyridoxine may be, in part, the result of a change in the immunogenetic balance between this tumour and this host. This change might occur either by a change of 'antigenicity' of the tumour, or by some alteration of the host responses to the tumour. Indeed, in either case, the development of *S*-180/B_6 may be somewhat similar to the changes in immunogenetic specificity and growth capacity of a tumour which have been observed during growth under various selective pressures[25].

The delayed emergence and gradual development of a tumour capable of growing in pyridoxine-depleted hosts is reminiscent of the pattern of growth observed during the development of drug resistance by a transplantable leukæmia[26]. This analogy suggests the possibility that a similar selection from a mixed population of cells has conditioned the development of *S*-180/B_6.

The development of this sub-line of *S*-180 provides experimental material for further study of the contribution of metabolic or immunogenetic factors to the altered growth capacity of a mammalian tissue.

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assays. This work was supported, in part, by research grants *CY*-2857 and *CY*-4130 from the National Cancer Institute of the United States Public Health Service.

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BIOCHEMISTRY OF BOVINE KETOSIS: THE THERAPEUTIC USE OF FUMARATE AND CYSTEAMINE

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THE principal biochemical symptoms of bovine ketosis are a high level of ketone bodies in the body fluids and a hypoglycæmia of variable severity; a considerably lowered hepatic glycogen-level has also been observed[1]. There are reasons for believing that the enforced milk production in the post-parturient animal imposes a severe strain on its carbohydrate and fat metabolism, and that ketosis constitutes an aggravation of this metabolic imbalance.

Suboptimal Reaction-rates in the Citric Acid Cycle. We have shown (ref. 2) that the citrate-level in the serum of ketotic animals is only approximately 20 per cent of the normal. As a working hypothesis, it was suggested that this finding could signify a diminished rate of condensation of acetyl coenzyme *A* with oxalacetate to form citrate (Fig. 1). In support of this, it will be seen from Fig. 2 that when the citric acid cycle was stimulated by injections of sodium fumarate into ketotic animals, the citrate concentration increased to attain a normal level. One of the principal reasons for such a diminished utilization of acetyl coenzyme *A* in the cycle was thought to be its competitive use for fat synthesis in the post-parturient animal. In this, at the peak of milk production, the utilization of acetyl coenzyme *A* for the formation of fat may take preference over that for citrate synthesis (Fig. 1). An over-production of acetyl coenzyme *A* through activation of large quantities of ruminal fatty acids by coenzyme *A* would, according to accepted views[3,4], lead to excess formation of ketone bodies; another contributing factor may be a diminished supply of reduced pyridine nucleotides (see below). Some evidence for the preferential direction of acetyl coenzyme *A* towards fat metabolism is provided by the accumulation of coenzyme *A* in the lactating gland[5]. Attempts were made to shift the equilibrium between the two competitive reactions of acetyl coenzyme *A* towards the citric acid cycle in the ketotic animal by administering fumarate, which would stimulate the cycle and, in particular, would provide an extra supply of oxalacetate for the condensation with acetyl coenzyme *A*. From Fig. 3 it will be seen that this treatment had the expected effect, namely, that the level of the ketone bodies in the serum was considerably reduced.

Although the diversion of the metabolism of acetyl coenzyme *A* from its oxidative path towards fat synthesis is considered to be one of the general causes of the apparent suboptimal reaction-rate in the cycle, there is also some evidence for an interference with two specific reactions in the cycle, namely, with the oxidation of pyruvate and with that of oxoglutarate (Fig. 1); for we have shown[2] that in bovine ketosis the levels of both these oxo-acids were several hundred per cent greater than normal and that that of succinate was considerably depressed. The idea of a retarded oxidation of these oxo-acids suggested itself. Both reactions proceed by a common unique mechanism and require the same

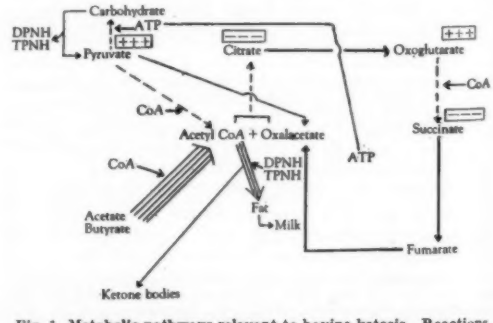

Fig. 1 Metabolic pathways relevant to bovine ketosis. Reactions represented by broken lines are believed to occur at suboptimal rates. +++, in rectangle, elevated serum levels; ———, in rectangle, depressed serum-levels

co-factors, among them coenzyme *A*. This, as pointed out above, is used in the post-parturient animal to a great extent for the activation of ruminal fatty acids and is partly lost through milk secretion[6,7]. These considerations led us to envisage the possibility that the interference with the oxidation of pyruvate and of oxoglutarate in ketosis may be caused by a reduced availability of coenzyme *A*. The idea is supported by the work of Peeters *et al.*[8], in which the authors showed a diminished acetylating power of ketotic cows, as ascertained by their excretion of acetylated sulphanilamide. Moreover, Gallagher[9] has recently demonstrated a subnormal level of coenzyme *A* in the livers of ewes suffering from ketosis. The above hypothesis was tested by injecting into ketotic animals small quantities of cysteamine, which in certain reactions possesses coenzyme *A* activity[10]. From Fig. 4 it will be seen that this treatment caused a rapid fall in the serum-levels of pyruvate and oxoglutarate. On the other hand, treatment with fumarate proved to be ineffective in this respect, leading to an even greater increase in the levels of pyruvate and oxoglutarate. This was to be expected if one accepted the view that fumarate stimulated the cycle without, however, overcoming the interference with the oxidation of the two oxo-acids.

Both forms of treatment, as shown in Figs. 2 and 3, led to a disappearance of the other abnormal biochemical symptoms investigated—cysteamine treatment more rapidly than fumarate treatment. Among

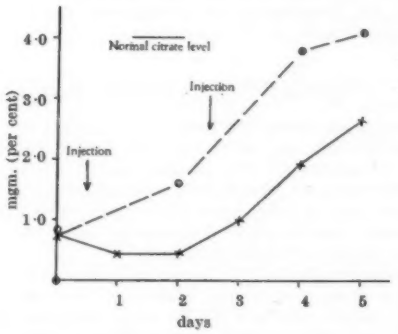

Fig. 2. Changes in the serum levels of citrate during treatment of cows suffering from ketosis with fumarate (20 gm. in 450 ml. water, injected subcutaneously), ———; and cysteamine (750 mgm. in 250 ml. water, injected intravenously), - - - -

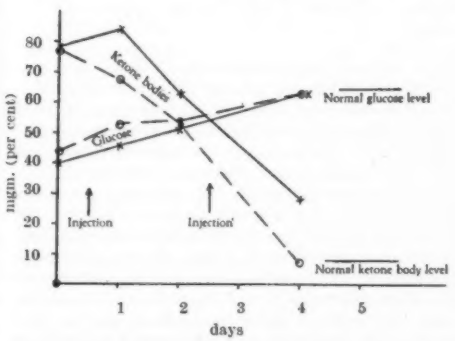

Fig. 3. Changes in the serum levels of glucose and ketone bodies during treatment of cows suffering from ketosis with fumarate, ———; cysteamine, - - - -. Dosages as in Fig. 2

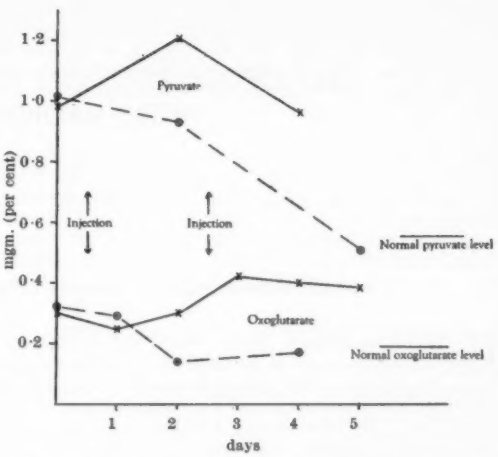

Fig. 4. Changes in the serum levels of pyruvate and α-oxoglutarate during treatment of cows suffering from ketosis with fumarate, ———; cysteamine, - - - -. Dosages as in Fig. 2

the symptoms of recovery was an immediate rise of the abnormally low level of glucose in the serum. These low levels may be caused by an interference with the adenosine triphosphate-requiring *synthetic* mechanism, since in bovine ketosis the *degradation* of glucose appears to be proceeding at a normal rate[11]. It can therefore be argued that an increase in the formation of adenosine triphosphate through stimulation of the cycle could raise the level of hepatic glycogen and that of blood glucose. Furthermore, with more glucose present for the purpose of degradation, more reduced pyridine nucleotides should become available for the reduction of acetoacetyl coenzyme *A*, which in turn would lead to a decrease in the level of ketone bodies, since an inverse relationship appears to exist between the degree of anaerobic degradation of carbohydrate and the accumulation of ketone bodies[12,13].

Therapeutic Experiments. Of 16 animals treated with sodium fumarate, 14 responded to the treatment and recovered within 7–10 days. All the 33 cases of primary ketosis treated with cysteamine responded rapidly and recovered within 3–6 days. Figs. 2–4 refer to pairs of animals which, for the sake of comparison, were selected for the similarity of the pre-treatment-levels of their serum components. However, the course of recovery shown in these graphs was very similar in all recorded cases, full details of which have been published elsewhere[14].

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SELF-DECOMPOSITION OF COMPOUNDS LABELLED WITH RADIOACTIVE ISOTOPES

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IT is quite evident that before an isotopically labelled compound can be profitably used its purity must be known. This will normally be determined following the preparation of the material and, if it is purchased, the information will be provided by the commercial supplier. However, if the material is not used at once, it may undergo significant decomposition under the influence of its own radiation, and there are some aspects of this problem of which we feel users of tracer compounds are insufficiently aware. It is true there is a substantial literature on radiation chemistry generally, but most of it is concerned with irradiation of solutions rather than of pure organic substances, while the actual phenomenon of radiation self-decomposition has been dealt with in relatively few papers[1–5]. The object of this article is to analyse the problem with particular reference to carbohydrates and to present some further quantitative information.

It is important to distinguish in what follows between a chemical and a radiochemical impurity, and to be clear what is meant by the latter. We define a radiochemical impurity as being any radioactive species other than the declared isotope in the stated position(s) of the given compound. In passing, we may note that it commonly happens that a small quantity of radiochemical impurity can be critical whereas a comparable amount of inactive impurity is unimportant.

Types of Self-decomposition

The decomposition of a compound labelled with a radioactive isotope can be due to one or more of four effects:

(i) Primary (internal) radiation effect, that is, the decomposition or transformation of a molecule caused by the disintegration of one of its unstable atomic nuclei. This atom, transformed into another element, might or might not be eliminated from the molecule. However, in either case, providing the daughter nuclei are stable, this will only give rise to a radiochemical impurity if the molecule contains a further radioactive atom.

(ii) Primary (external) radiation effect, that is, the decomposition or transformation of a molecule by interaction with a nuclear particle. If the molecule is a labelled one, this will contribute to the radiochemical impurity.

(iii) Secondary radiation effect, that is, the decomposition or transformation of a molecule of the labelled compound due to its reaction with reactive species, for example, free radicals, produced as a result of primary radiation decomposition. The reactive species may not necessarily be produced from the labelled compound but from its environment, for example, residual water in freeze-dried samples.

(iv) Chemical effect, that is, the decomposition or transformation of the radioactive material caused by chemical reactions which are not connected with radiation. Clearly, this is a hazard faced by any chemical compound, but it may be more probable in the case of a labelled one for several reasons. First, in an effort to obtain a good yield of material of high specific radioactivity, the highest chemical purity is not always achieved, and it is often difficult or expensive to determine this purity. The impurities may then react with the compound. Further, the small amount—possibly only a few micrograms—of radioactive material which is commonly synthesized or distributed by suppliers may suffer chemical decomposition in unexpected ways which would not normally be observed with larger quantities. It could be due, for example, to the atmosphere above a solid, or non-inertness of the container.

Magnitude of the Radiation Effects

The magnitude of the primary (internal) effect can be calculated in any particular case from the available data. Commonly it is a greater practical concern to know the amount of radiochemical impurity produced, and this can be calculated if the pattern of labelling is known. An example of this is given in the subsequent section on macromolecules.

One of the factors influencing the amount of decomposition due to primary (external) and secondary effects is the fraction of its own radiation energy absorbed by the labelled material. For a pure β-emitter distributed over a relatively large area in a layer of even thickness l (cm.) this fraction, F, is given by:

$$F = \frac{pl}{2r}\left(1{\cdot}5 + \ln\frac{r}{pl}\right)$$

where p is the density (mgm. cm.$^{-3}$) and r is the mean range of the particles, expressed in mgm.cm.$^{-2}$ units. In this it is assumed that $r \ll pl$ and that all particles have the energy corresponding to their mean energy. A more exact value may be obtained for definite values of p and l using a known beta-spectrum, but the error is generally small. No allowance is made for back-scatter from the container or for edge effects, though for a given area these latter will, of course, be of increasing significance with increasing energy of the β-particle. The calculation involves determination of the average range of a β-particle by a double integration, the first for the solid angle around a point in a layer of the material, and the second for the contribution of all layers throughout the thickness of the solid.

The magnitude of decomposition (per cent) due to the primary (external) radiation effect is $\{1 - \exp(-F\epsilon a s_0 t \cdot 6{\cdot}14 \times 10^{-16}\}\ 100$, where F is the fraction of its own radiation energy absorbed by the compound, ϵ is the mean energy of the radiation in electron-volts, a is the number of molecules irreversibly damaged per 100 eV., s_0 is the initial specific radioactivity of the compound in curies/mole, and t is the time in seconds. For compounds labelled with relatively short-lived isotopes, the term t in this expression should, of course, be replaced by $1/\lambda\ \{1 - \exp(-\lambda t)\}$, where λ is the radioactive decay constant.

Remedial Measures

It is clearly desirable to reduce the magnitude of decomposition of labelled compounds to a minimum. Setting aside the decomposition due to the primary (internal) radiation effect as being beyond control, we can consider the possible remedies for the other three types of decomposition.

Considering decomposition due to the chemical effect first, it is evident that the highest possible degree of freedom from harmful impurities is desirable, consistent with the requirements for specific radioactivity. Storage under vacuum is a common and useful precaution. Attention should also be paid to the inertness of the storage vessels, particularly for liquids or freeze-dried syrups. In our experience the alkalinity of normally washed 'Pyrex' glass is detrimental to the stability of carbon-14 carbohydrate syrups. Storage at as low a temperature as possible can also help by reducing the rate of otherwise unavoidable chemical reactions.

The two fundamental methods for reducing the magnitude of primary (external) radiation decomposition are dispersion over a large area and dilution.

As already pointed out, the fraction of its own radiation energy absorbed by a radioactive compound distributed over a relatively large area is dependent on the thickness and density of the layer. Thus, the principle of such dispersion is to ensure that the nuclear particle escapes from the body of the radioactive material with the minimum interaction on the way. This method has been widely utilized in storage of labelled compounds—particularly for small quantities at high specific radioactivities—but frequently the material may need to be distributed over an area too large to be practical in order to reduce the self-irradiation to a satisfactory level.

The object of dilution is to interpose inactive molecules in the path of the radiation. This can be achieved either by adding the inactive form of the compound itself or by introducing other substances. The former avoids the necessity of subsequent isolation of the radioactive compound, but as it involves a drop in specific radioactivity it is not always acceptable.

It is not possible to suggest a universal method which will prevent the decomposition due to secondary radiation effects. However, it is evident that either dispersion over an area or dilution with the substance itself will reduce this type of decomposition, but the effect of dilution with a foreign substance will depend on the nature of that substance. On the credit side it will absorb radiation which might produce radioactive impurities, and in certain cases it may terminate chain reactions which would otherwise result in substantial decomposition following the radiolysis of a few radioactive molecules[6,7]. Conversely, if unwisely chosen, it may produce, by interaction with the radiation, reactive species which will interact with the labelled compound, and so do more harm than good. It is important to appreciate how wide is the range of susceptibilities to radiation for different compounds[4]. Storage of radioactive materials at low temperatures will usually reduce the decomposition due to secondary radiation effects, but will not, in general, completely prevent it. A high standard of chemical purity, already stressed for another reason, may also reduce this decomposition, since, although the impurity may not be harmful in itself, the products of its interaction with the nuclear particles may be. An example of such an impurity is water in the case of carbohydrates.

Observations on Carbon-14 Carbohydrates

The stabilities of samples of uniformily labelled [^{14}C]-sucrose and D-[^{14}C] glucose with relatively high specific radioactivities are shown in Table 1. The compounds were prepared by photosynthesis, purified by ion-exchange and paper chromatography and finally crystallized. No radiochemical impurity was detected in either case by reverse isotope dilution analysis, and their chromatographic radiochemical purities were both found to be 99·9 per cent. After being dispensed from aqueous solutions, samples were stored in the freeze-dried form or uniformly distributed on Whatman No. 3 paper. In either case they were contained in 'Pyrex' tubes which had been filled with water and autoclaved for 2 hr. at 15 lb./sq. in. to remove surface alkalinity. The tubes of those samples which were stored *in vacuo* were evacuated to a pressure of 0·01 mm. mercury for several hours before being sealed in order to reduce the moisture content to a minimum.

The radiochemical impurities produced during storage were determined by scanning of paper chromatograms. Spots with R_F values corresponding to those of glucose and fructose were the principal impurities in the case of sucrose.

Many other experiments covering a wide range of specific radioactivities have shown that, under given storage conditions, the amount of decomposition is proportional to the specific radioactivity, provided that the substance is not allowed to decompose too far.

A comparison of tubes 7–10 suggests that, in at least the first three of these, secondary radiation effects take a major role in the decomposition. This is perhaps not surprising, since freeze-dried glucose will retain non-bonded water as 'impurity'. Sucrose, on the other hand, can with efficient freeze-drying techniques be obtained anhydrous, and the small difference in magnitude of decomposition between tubes 1 and 2 suggests that in these cases decomposition is to a great extent due to primary radiation effects. This view is supported by the relatively high calculated value for the apparent energy required to disrupt one molecule (24 eV. for tube 2). By the same criterion the most stable freeze-dried glucose sample (tube 10) is probably still greatly susceptible to decomposition due to secondary radiation effects.

It is clear from the high $G(-M)$ values for tubes 3–6, 11, 12, that such decomposition as does occur when radioactive sugars are distributed on paper is due to secondary radiation effects, probably as a result of the moisture content of the paper. However, under optimum conditions, the overall magnitude of decomposition is markedly reduced by storage under such conditions and so, since it is easy to recover the sugar quantitatively, this method is now used to facilitate

Table 1. Self-decomposition of [^{14}C]-Sucrose and D-[^{14}C] Glucose

Compound	Tube No.	Storage conditions: Form	Temp.	Pressure	Impurity observed (per cent)	Initial decomposition per year per mc./mM (per cent)	Average mass per unit area (freeze-dried) (mgm./cm.^{2})	Area of paper (cm.^{2}) (d)	Energy absorbed by sugar or sugar syrup ($F \times 100$) (per cent) (e)	$G(-M)$ value (f)
Sucrose (a, b)	1	Freeze-dried	Room	Vac.	16·4	0·071	0·35	—	16	4·6
	2	Freeze-dried	−80° C.	Vac.	15·1	0·065	0·35	—	16	4·2
	3	On paper	Room	Atm.	15·7	0·068	—	21	0·3	234
	4	On paper	−80° C.	Atm.	4·9	0·020	—	21	0·3	68
	5	On paper	Room	Vac.	2·4	0·010	—	21	0·3	33
	6	On paper	−80 °C.	Vac.	1·8	0·007	—	21	0·3	25
Glucose (c)	7	Freeze-dried	Room	Atm.	18·9	0·77	0·2	—	10	79
	8	Freeze-dried	−80° C.	Atm.	6·0	0·23	0·2	—	10	23
	9	Freeze-dried	Room	Vac.	13·1	0·51	0·2	—	10	53
	10	Freeze-dried	−80° C.	Vac.	3·6	0·133	0·2	—	10	14
	11	On paper	Room	Vac.	1·2	0·044	—	47	0·05	900
	12	On paper	−80° C.	Vac.	0·7	0·026	—	47	0·05	526

(a) Each tube of sucrose contained 500 μc. in 1·16 mgm. sucrose (149 mc. per m.mole; abundance of carbon-14 19·5 per cent) and was stored for 88 weeks. Calculation shows that primary (internal) radiation decomposition contributed 0·05 per cent to the observed impurity.

(b) Other experiments with samples of freeze-dried sucrose have shown that at −80° C. decomposition is considerably increased if the sugar is stored under atmospheric pressure instead of being sealed under vacuum. The difference is even greater with samples held at room temperature.

(c) Each tube of glucose contained 100 μc. in 0·43 mgm. glucose (42 mc. per m.mole; abundance of carbon-14·11·0 per cent) and was stored for 34 weeks. Calculation shows that primary (internal) radiation decomposition contributed 0·005 per cent to the observed impurity.

(d) The weight of the Whatman No. 3 paper was 18 mgm. cm.$^{-2}$.

(e) The fraction of the energy absorbed by the sugar or sugar syrup was calculated either (i) by using the relationship deduced above, although the geometry is some way from the ideal; or (ii) by assuming the compound and the paper to absorb all the radiation in the ratio of their weights.

(f) Defined as the number of molecules permanently altered or decomposed per 100 eV. absorbed by the sugar or sugar syrup.

the supply of carbohydrates with high specific radioactivities from the Radiochemical Centre.

An example of the varied decomposition by secondary radiation effects was recently observed by us. [^{14}C]-dextran sulphate containing c. 20 glucose units per molecule was prepared by sulphation of an appropriate [^{14}C]-dextran hydrolysate. It had the relatively low specific radioactivity of 22·4 mc. per gm. atom of carbon (c. 3 mc./m.mole dextran sulphate). It was stored in the freeze-dried form, but when inspected after three weeks it was charred and became a total loss, whereas inactive dextran sulphate did not decompose during storage for several months. The decomposition of the labelled dextran sulphate was presumably due to a secondary radiation effect arising from the prior liberation of sulphuric acid. The sulphuric acid, being fortified rather than diluted in the process, destroyed the rest of the material.

Macromolecules

We quoted earlier an expression for the magnitude of the primary (external) effect which includes a term for specific radioactivity, s_0, expressed in curies per mole. While it is, of course, true for all compounds, it is particularly important when dealing with macromolecules to appreciate that this term needs to be expressed on a molar, and not on a unit weight, basis. To illustrate this we may consider the case of some glucose, maltose and amylose (containing n glucose units), all prepared from [^{14}C]-carbon dioxide of the same specific radioactivity, and stored under identical conditions, so that the irradiation per unit mass is the same in each case. It is clear that for each destructive interaction between a β-particle and a carbohydrate molecule the impurity produced will contain x, $2x$, and nx atoms of carbon-14 respectively in the three cases. Nevertheless, if we hydrolyse such partially decomposed samples, the resultant glucose will have the same purity in each case, neglecting any effects due to other causes.

How secondary effects will vary with increasing chain-length will depend on what the result of the particular effect is. In some cases the above principle will hold, whereas in others—such as attack on reducing end-groups—it will not.

It is sometimes necessary to consider the contribution of the primary (internal) effect to the production of radiochemical impurity from a labelled macromolecule. This will depend, of course, on the pattern of labelling. For example, in a polysaccharide prepared directly from [^{14}C]-carbon dioxide, so that the labelling is statistically uniform throughout all its molecules, the number of radioactive atoms in the form of an impurity initially produced per nucleus disintegrating is the multiple of its isotopic abundance expressed as a fraction and $(n - 1)$, where n is the number of atoms of the given element in the molecule. Production of radiochemical impurity due to this cause, will, of course, fall exponentially with time, as nuclei in the resultant impurity themselves disintegrate; but it is important to appreciate that a similar compound, prepared from [^{14}C]-carbon dioxide at twice the specific radioactivity, and then diluted with an equal weight of inactive carrier, will produce a different amount of radiochemical impurity as a result of the primary (internal) effect, even though its pattern and degree of labelling appears superficially to be identical with the compound first mentioned.

The amount of radiochemical impurity arising as a result of this effect can be surprisingly large with macromolecules, even when the isotope has a long half-life. For example, a glucose polymer containing 1,000 glucose units, and prepared from [^{14}C]-carbon dioxide having the same isotopic abundance as that used to prepare the sucrose quoted in Table 1, would give rise to 0·28 per cent of radiochemical impurity in one week as a result of this effect.

Conclusion

We have not attempted to give a comprehensive review of this subject. We have rather aimed at

illustrating certain principles and have endeavoured to show that material of very high specific radioactivities can be used, and even stored, under certain conditions, but that a constant awareness of the phenomenon is called for on the part of all users of compounds labelled with radioactive isotopes.

We are indebted to Prof. E. J. Bourne, Dr. J. R. Catch, and Dr. J. S. Glover for helpful discussions.

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TRACE ELEMENTS IN AUSTRALITES

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THE chemical composition of tektites can provide much evidence about their origin. The concentrations of the major elements have been known within close limits for many years, although for some of the constituents present in low amounts, for example, sodium monoxide, the data are of poor quality[1]. A few determinations have been made of the elements present in trace quantities. Among the early investigations are those of Preuss[2,3] and Heide[4–6]. More recent determinations have been of rubidium[7,8], uranium[9,10], thorium[9], lithium, rubidium and cæsium[11] and of several elements by Cohen[12]. None of these data, except for the lithium and rubidium figures given by Cohen[12] (see Taylor[11]) is very different from terrestrial abundances, and gives any support to theories requiring an extra-terrestrial or extra-solar system origin for these interesting glassy objects. Many of the reported determinations have been carried out as a sideline to other work, or to provide evidence on a particular point, examples being the nickel and chromium determinations of Preuss[2,3]. No systematic study of one group appears to have been carried out.

In collaboration with R. D. Cherry of the Physics Department of this University, we have been studying the composition of a group of australites kindly provided by the South Australian Museum, Adelaide. The australites are a singularly suitable group for study. They cover a wide area (2×10^6 miles^2); occur, with minor exceptions, on the present surface; have been melted less than 10^6 years ago, on the basis of recent potassium–argon ages[13]; show well-preserved evidence of two periods of melting, and cover a wider range in chemical composition than any other group. Evidence is accumulating that they display a regional variation in composition[11,14].

Determinations have been completed of trace elements on 14 australites using emission spectrochemical methods of analysis following the methods outlined by Ahrens and Taylor[15]. Because of the current interest in the origin of tektites, averages of these results are presented here (Table 1) and briefly discussed in this preliminary account. The analytical techniques for the alkali elements have been described elsewhere[11]. Copper and gallium were determined using sodium as a variable internal standard, utilizing the similar volatilization behaviour of these elements in the d.c. arc. Anode excitation was employed throughout. The remaining elements, which are relatively involatile under these conditions, were determined using palladium as an internal standard. All determinations were made in duplicate, and the wave-length range of 2470–9600 Å. was covered, with a total of four exposures using Kodak 103-0 and *IN* plates. Spectrochemical determinations are particularly liable to systematic bias and it is mandatory to employ standard samples for calibration as close as possible in composition to the samples being analysed. The interlaboratory rock standards, *G*-1 (granite) and *W*-1 (diabase)[16], were selected as the most suitable. In general, they bracket the composition of the australites, and differ only in being composed of discrete minerals, in contrast to the glassy tektites. The effect of this difference has not been evaluated, but is believed to be small. Most difficulties due to matrix difference in spectrographic analysis using the d.c. arc arise from the presence of different anions in samples and standards. In fact, the d.c. arc emission spectra of the australites over the entire wave-length range bear a general resemblance to a mixture of these standards, which represent, of course, the two common igneous rock types.

The results are given in Table 1. The average of all the fourteen samples is given, with the extremes of the range in composition. The spread in composition is also expressed as a relative deviation, *C* (per cent standard deviation), and this should be compared with the analytical precision for individual determinations, given in the same units. It can be seen that the range in composition is greater than the precision of individual determinations, indicating that there are real differences in composition between individual samples[11]. The detection limits for the spectrochemical methods used are also given. Those elements for which no data are given were sought, but if present, are below the detection limits given. Table 1 also contains figures for the average abundances of the elements in igneous rocks (commonly referred to as the crustal abundance) from Ahrens and Taylor[15], in chondritic meteorites from Goldschmidt[17] (with later additions) and in shales. We wish to direct attention to the general similarity between the abundances of the trace elements in australites, and the average abundance of these elements in the Earth's crust.

Cherry and Taylor[18] suggested that the average major element composition of tektites can be closely matched by a mixture of one part quartz with three parts of the non-volatile constituents of shales. It is

Table 1. A Comparison of the Abundances of Trace Elements in Chondritic Meteorites, Igneous Rocks, and Shales with Averages from Fourteen Australites

Element	Chondrites (17) p.p.m.	Igneous rocks (15) p.p.m.	Shales (19) p.p.m.	Australites				Spectrographic detection limit p.p.m.
				Average p.p.m.	Range p.p.m.	Relative deviation $C(\%)$	Analytical precision $C(\%)$	
Ag	0·09	0·08	—	—				0·5
As	2	2	—	—				100
Au	0·10	0·002	—	—				10
B	1·5	3	—	—				10
Ba	8	1,000	570	655	570–805	9·5	7·7	3
Be	1	2	—	—				30
Bi	0·002	0·2	—	—				10
Cd	0·5	0·15	—	—				10
Ce	0·52	46	—	—				100
Co	800	20	18	16	13–20	10·4	9·2	2
Cr	2,200	100	110	52	35–73	22·4	9·5	1
Cs	0·13	5	5[23]	2·7	1·4–4·2	34·6	9·9	1
Cu	90	55	18	7·0	5·2–8·6	15·4	13·2	0·5
Ga	5·3	19	13[24]	8·6	6·7–11·4	16·5	7·0	3
Ge	10	1·1	—	—				5
Hg	0·10	0·08	—	—				100
In	<0·001	0·11	—	—				1
La	0·33	18	—	—				50
Li	2·7	32	55	42	37–52	11·0	7·6	0·5
Mn	1,900	1,000	620	800	670–955	11·6	7·1	5
Mo	1·5	1	—	—				10
Nb	0·5	24	—	—				30
Nd	0·63	24	—	—				10
Ni	13,400	35	64	30	25–50	22·1	4·1	5
Pb	0·65	15	20[21]	—				20
Pd	1·5	0·004	—	—				10
Pt	2·0	0·005	—	—				50
Rb	3·7	115	140[22]	84	65–99	12·1	8·3	1
Sb	0·1	0·1	—	—				20
Sc	9·4	20	14	12	8·9–16	15·6	12·5	2
Sn	1	2	—	—				20
Sr	10	450	300[20]	195	150–265	16·8	10·8	5
Th	0·03	10	—	—				100
Ti	790	4,400	4,920	4,280	3,040–5930	21·4	7·5	10
Tl	0·0014	0·8	—	—				1
U	0·05	3	—	—				100
V	39	110	120	75	58–94	14·6	5·4	5
W	—	2	—	—				20
Y	5	28	45	—				20
Yb	0·19	3	—	—				10
Zn	180	40	—	—				100
Zr	33	156	160[22]	470	370–555	12·6	7·9	10

difficult to establish average values for trace elements in shales, but Shaw[19] has considered many of the problems and his data are used, except where indicated. More recent data for strontium[20], lead[21], zirconium[22], rubidium and cæsium[23], and gallium[24] are used to supplement Shaw's results. In general, the trace element data in australites are consistent with derivation from a quartz-shale mixture in which shale is the major component. The relatively higher amount of zirconium in the australites in comparison with shales may well be derived from small quantities of the resistant mineral zircon accompanying the quartz.

In conclusion, the data for chromium, nickel and cobalt given here lend no support to a derivation of tektites from meteorites, or from meteorite collisions with the Earth, or from the Moon. From considerations of the structure and density of the Moon, its overall composition is probably close to that of the chondrites. Material from the lunar surface is probably similar to that in the interior, since there seem to be no selenological processes comparable to geological ones. In addition, the surface material can be expected to be rather rich in nickel and cobalt from meteoritic collisions, and hence rather easily distinguished from terrestrial rocks. Extra-terrestrial theories for the origin of tektites must provide for the duplication of many geological processes to account for the overall pattern of trace element distribution.

Data for the individual samples, together with details of the analytical methods and determinations of the major elements by Dr. H. B. Wiik, will be discussed at length in a subsequent paper.

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A MATHEMATICAL MODEL FOR GAS-LIQUID PARTITION CHROMATOGRAPHY

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THE widespread adoption of gas-liquid partition chromatography for the separation of complex mixtures has led to much speculation with regard to the mechanism of separation. Plate theories of separation have been considered by Martin and Synge[1], Mayer and Tompkins[2], and Glueckauf[3], while continuous or rate theories have been developed by Boyd, Adamson and Myers[4], Lapidus and Amundson[5], Glueckauf[6], Klinkenberg[7], Tunitskii[8], Giddings and Eyring[9] and by van Deemter, Zuiderweg and Klinkenberg[10]. Keulemans[11] has summarized the major results obtained by both theories of chromatography. The model discussed in this article essentially includes most of the previous continuous models with the further inclusion of the effects of non-linear solubility and column pressure drop. The use of arbitrary overall mass transfer coefficients has been avoided by separating the resistance to mass transfer into two parts, one due to the gas film and the other due to the liquid film. The describing partial differential equations are :

$$\frac{\partial X}{\partial t} = E\frac{\partial^2 X}{\partial z^2} - \left(u - \frac{2E}{P}\frac{\partial P}{\partial z}\right)\frac{\partial X}{\partial z} - \frac{k_G RTA}{\varepsilon}(X - X_i) \quad (1)$$

$$c_i = K_1 X_i P + K_2 X_i^2 P^2 \quad (2)$$

$$\frac{\partial c}{\partial t} = D_L \frac{\partial^2 c}{\partial y^2} \quad (3)$$

where $X(z,t)$ is the mole fraction of solute in the gas phase, $X_i(z,t)$ the mole fraction at the gas-liquid interface, $c(y,z,t)$ the concentration of the solute in the stationary liquid phase, $c_i(z,t)$ the concentration at the gas-liquid interface, z the axial distance along the column, y the distance in the liquid film, t is time, $u(z)$ is the average gas velocity through the voids in the packed bed, $P(z)$ the total pressure, T the uniform column temperature, R the gas constant, k_G the 'Whitman' gas-film coefficient[12], E the longitudinal dispersion coefficient (cf. Taylor[13]), ε the void fraction, D_L the diffusivity of the solute in the liquid phase, and A is the area of the gas-liquid interface per unit volume of packed bed. The constants K_1 and K_2 are empirical constants in the solubility relationship.

Equation (1) accounts for diffusion in the gas phase, equation (2) represents a nonlinear equilibrium relationship between the gas and liquid phases, and equation (3) is a statement of molecular diffusion in the partitioning liquid. If the liquid film is thin and $c_m(z,t)$ is the concentration at a point midway in the liquid film, then equation (3) can be approximated by the following differential-difference equation :

$$\frac{\partial c_m}{\partial t} = \frac{D_L}{\Delta y^2}(c_i - c_m) \quad (4)$$

where Δy is half the liquid film thickness.

Numerical Solution of Equations

Equations (1), (2) and (4) have been solved numerically on the IBM 704 digital computer using finite difference techniques. The inset of Fig. 1 shows the conditions for an initial value problem in which a slug of solute of mole fraction $\bar{X}$ and length L_1 is suddenly introduced into a carrier gas stream at time $t = 0^+$ by simultaneously opening two gates. The initial conditions for this case are then :

$$X(z,0) = \begin{cases} \bar{X}, & 0 < z < L_1 \\ 0, & z > L_1 \end{cases} \quad (5)$$

$$\left.\begin{aligned} X(z,0) = X_i(z,0) = 0 \\ c(z,0) = c_m(z,0) = 0 \end{aligned}\right\} L_2 < z < L_3 \quad (6)$$

and the boundary conditions are :

$$\text{gas velocity} = \begin{cases} u, & L_2 < z < L_3 \\ u\varepsilon, & z < L_2 \text{ and } z > L_3 \end{cases} \quad (7)$$

$$\text{gas film coefficient} = \begin{cases} k_G, & L_2 < z < L_3 \\ 0, & z < L_2 \text{ and } z > L_3 \end{cases} \quad (8)$$

A study of the parameters that affect gas-liquid chromatography has been made using the computer programme and considering the particular case of the elution of a pure *iso*butylene slug with argon using dinonyl phthalate as the stationary phase, the column temperature and pressure being 25° C. and 1 atm. throughout. The data were as follows : $L_1 = 5$ cm., $L_3 - L_2 = 50$ cm., $L_2 - L_1 = L - L_3 = 1$ cm., $u = 5$ cm./sec., $A = 131{\cdot}2$ cm.^{2} per cm.^{3}, $\Delta y = 7{\cdot}0 \times 10^{-5}$ cm., $K_1 = 1{\cdot}14 \times 10^{-3}$ gm.-mole per cm.^{3} atm., $D_L = 6{\cdot}7 \times 10^{-7}$ cm.^{2} per sec. (cf. Funk[14] and Kesten[15]), $k_G = 10^{-5}$ gm.-mole per cm.^{2} sec. atm. Unless otherwise specified, E was taken to be equal to the molecular diffusion coefficient of *iso*butylene in argon (0·0674 cm.^{2} per sec.) as calculated by the method of Hirschfelder, Bird and Spotz[16].

Below a value of about 10^{-5} gm.-mole per cm.^{2} sec. atm., k_G was found to affect strongly both the retention time and the shape of the elution curve. However, above a value of 10^{-5}, k_G has no effect on the elution curve, indicating that in order to effect good separations, diffusion-rates through the gas film must be high. Fig. 1 clearly demonstrates that the effect of large longitudinal dispersion coefficients is to broaden the elution curve and therefore reduce the resolution without affecting the retention time.

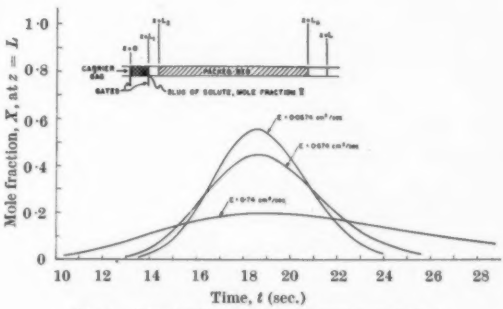

Fig. 1. Effect of longitudinal dispersion coefficient

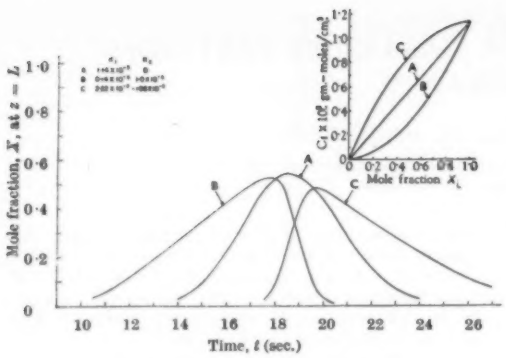

Fig. 2. Effect of non-linear solubility

Fig. 2 demonstrates that the effect of a nonlinear solubility relationship is to induce considerable skewness and tailing in the elution curve with a consequent displacement of the peak. The direction of tailing is obviously coupled to the nature of the nonlinearity.

Analytical Solution of Equations

For the special case of uniform column pressure ($\partial P/\partial z = 0$) and linear solubility ($K_2 = 0$), equations (1), (2) and (4) have been solved analytically by a transform method similar to that of Lapidus and Amundson[5]. The result, however, was found to be unwieldy; in this respect the numerical solution is easier to use and also accounts for the effects of nonlinear solubility and pressure drop.

Since the numerical solution shows that longitudinal diffusion has no effect on the retention time but only affects the sharpness of the band, the effect of physical properties on the retention time may be obtained by solving equations (1), (2) and (4) with the assumptions that $E = 0$, $\partial P/\partial z = 0$ and $K_2 = 0$, subject to the initial conditions (6) and the following boundary conditions:

$$X(0,t) = \begin{cases} 0, & 0 < t \\ \overline{X}, & b > t > 0 \\ 0, & t > b \end{cases} \qquad (9)$$

A solution to this boundary value problem was obtained by Laplace transform methods and reads:

$$\frac{X(L,t)}{\overline{X}} = \begin{cases} 0, & 0 < t < L/u \\ \displaystyle\int_{t-b}^{t} \exp\left(-\alpha\left(\tau - \frac{L}{u}\right)\right) \exp\left(-\frac{L}{u}\beta\right)\sqrt{\frac{\alpha\beta L/u}{\tau - \frac{L}{u}}}\, I_1\left[2\sqrt{\alpha\beta\frac{L}{u}\left(\tau - \frac{L}{u}\right)}\right] d\tau, & t > \frac{L}{u} \end{cases} \qquad (10)$$

where

$$\alpha = \frac{D_L}{\Delta y^2}\left[\frac{k_G}{\frac{D_L K_1}{\Delta y} + k_G}\right] \text{ and}$$

$$\beta = \frac{k_G R T A}{\varepsilon}\left[\frac{\frac{D_L K_1}{\Delta y}}{\frac{D_L K_1}{\Delta y} + k_G}\right] \qquad (11)$$

The modified Bessel function of first order, I_1, can be approximated by an asymptotic expansion if $2\sqrt{\alpha\beta\frac{L}{u}\left(\tau - \frac{L}{u}\right)} > 10$ so that equation (10) becomes:

$$\frac{X(L,t)}{\overline{X}} = \frac{(\alpha\beta L/u)^{\frac{1}{2}}}{2\sqrt{\pi}} \int_{t-\left(\frac{L}{u}+b\right)}^{t-\frac{L}{u}} \frac{\exp\left(-\left(\sqrt{\alpha}\sqrt{\tau - \frac{L}{u}} - \sqrt{\beta\frac{L}{u}}\right)^2\right)}{\left(\tau - \frac{L}{u}\right)^{\frac{3}{2}}} d\tau, \; t > \frac{L}{u} \qquad (12)$$

Investigation of equation (12) has shown that it is valid for most conditions experienced in gas-liquid chromatography. Since we are only interested in the retention time a further approximation can be made by reducing the duration of the pulse, b, when equation (12) becomes:

$$\frac{X(L,t)}{\overline{X}} = \frac{b(\alpha\beta L/u)^{1/4}}{2\sqrt{\pi}\left(t - \frac{L}{u}\right)^{3/4}} \exp\left(-\left(\sqrt{\alpha}\sqrt{t - \frac{L}{u}} - \sqrt{\beta\frac{L}{u}}\right)^2\right) \qquad (13)$$

The retention time, t_R, is the time at which the above function maximizes, so that:

$$t_R = \frac{L}{u}\left[1 + \frac{K_1 R T A \Delta y F}{\varepsilon}\right] \qquad (14)$$

where:

$$F = \frac{1}{2} - \frac{3u}{4\beta L} + \frac{1}{2}\sqrt{1 - \frac{3u}{\beta L}} \qquad (15)$$

In cases where the liquid film is thin and the column is long, F has a value very close to unity and the volume V of stationary liquid per unit volume of column is $2A\Delta y$ so that:

$$t_R = \frac{L}{u}\left[1 + \frac{K_1 R T V}{2\varepsilon}\right] \qquad (16)$$

The so-called 'apparent' retention time, t'_R, can be obtained by subtracting the transport time L/u from (16), therefore:

$$t'_R = \frac{L K_1 R T V}{2u\varepsilon} \qquad (17)$$

Furthermore, if the liquid solution is ideal, K_1 can be calculated by Raoult's law and the vapour pressures of the solute represented by the Clausius–Clapeyron equation, so that:

$$t'_R = \frac{L\rho_m R T V}{2p^0 u\varepsilon} = \frac{L\rho_m R T V \exp(\Delta H/RT)}{2Bu\varepsilon} \qquad (18)$$

where p^0 is the vapour pressure of the solute at the column temperature, ρ_m the molal density of the liquid phase, ΔH the latent heat of vaporization of the solute and B is a constant in the Clausius–Clapeyron equation.

Equation (18) predicts that the 'apparent' retention time is proportional to the volume of stationary liquid and the column length, inversely proportional to the vapour pressure of the solute, and independent of the absolute column pressure provided the carrier

gas velocity is constant. The retention time should also be inversely proportional to the carrier gas velocity. Furthermore, according to (18), a plot of $\ln(t'_R/T)$ against $1/T$ will be a straight line. All the above predictions are observed experimentally and discussed by Keulemans[11]. The detailed comparison of the above theory with experiment will be discussed in further communications.

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EFFICIENCY OF SEPARATION IN BUFFERED PAPER CHROMATOGRAPHY OF ORGANIC ELECTROLYTES

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In chromatographic methods the efficiency of separation of a system in respect to a given binary mixture depends mainly on two parameters: (1) the number of theoretical plates, which determines the spread of a zone; (2) the selectivity, which determines the distance between two zones.

The latter parameter is usually expressed by the separation factor, which may be defined, for example, as the ratio of the distribution coefficients of the two substances to be separated (liquid–liquid extraction), or the ratio of the retention times (gas–liquid partition chromatography), etc. In paper chromatography it is most conveniently expressed as the difference between the R_F values of the substances under study ($\Delta R_F \geqslant 0$).

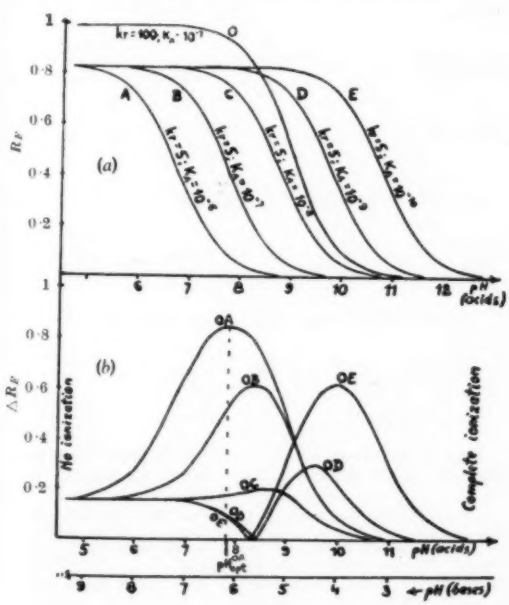

Fig. 1

In the case of organic electrolytes which in un-ionized form give high R_F values (near 1), improved separation may often be obtained by changing the pH of the water phase[1]. Fig. 1*a* illustrates the variation of the R_F values of a number of substances; in Fig. 1*b*, curves for ΔR_F as a function of pH are presented, which were obtained by subtracting the ΔR_F values of different pairs of substances at the same pH; for example, curve OA shows the variation of the ΔR_F of components O and A with change of pH of the water phase. It can be seen that often a maximum occurs on $\Delta R_F = f(p\mathrm{H})$ curves; the pH value at which this maximum is obtained may correspond to conditions of optimum efficiency of separation (highest possible differences in R_F values) for the pair of components considered. This optimum pH may be calculated by equating the derivative $\mathrm{d}\Delta R_F/\mathrm{d}p\mathrm{H}$ to zero; thus, taking into account the formulæ derived by Waksmundzki and Soczewiński[2]:

$$\frac{\mathrm{d}\Delta R_F}{\mathrm{d}p\mathrm{H}} = \frac{\mathrm{d}}{\mathrm{d}p\mathrm{H}}\left(\frac{\frac{k'r}{K'_A}}{\frac{k'r+1}{K'_A}+10^{p\mathrm{H}}} - \frac{\frac{k''r}{K''_A}}{\frac{k''r+1}{K''_A}+10^{p\mathrm{H}}}\right) = 0 \quad (1)$$

where k is partition coefficient of un-ionized substance; r is ratio of volumes of mobile and fixed phases; (kr is partition number of un-ionized substance[3]); K_A is ionization constant of acid. The indices $'$ and $''$ denote first and second component, respectively.

Solution of (1) gives:

$$p\mathrm{H}_{\mathrm{opt}} = \log \frac{\frac{k'r+1}{K'_A}\sqrt{\frac{k''r}{K''_A}} - \frac{k''r+1}{K''_A}\sqrt{\frac{k'r}{K'_A}}}{\sqrt{\frac{k'r}{K'_A}} - \sqrt{\frac{k''r}{K''_A}}} \quad (2)$$

The case for $kr \geqslant 100$. In buffered paper chromatography, the partition numbers kr of the un-ionized substances to be separated often are high, for example, 100 or more; hence the limiting R_F values (when

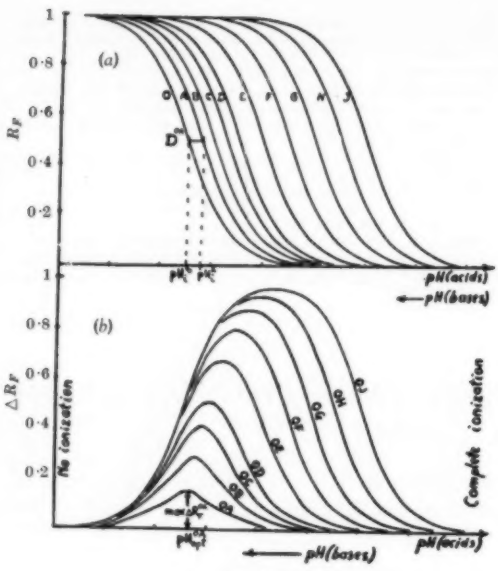

Fig. 2

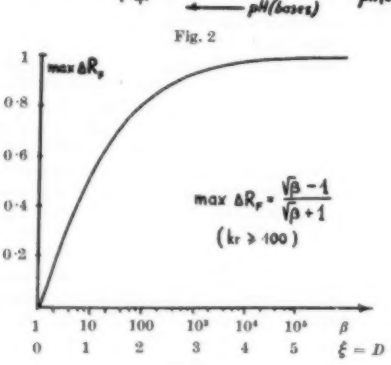

Fig. 3

substances are un-ionized) are greater than 0·99—the substances migrate with the front of the developing solvent. In those cases the shapes of the R_F vs. f(pH) curves are invariable and independent of the parameters K_A and kr, which influence only the positions of the curves. The inflexion point, which lies at the half-height of the curve (R_F about 0·5) and is the centre of axial symmetry of the curve, lies then at the pH value given by the formula :

$$pH_i = pK_A + \log(kr + 1) \approx pK_A + \log kr = \log \frac{kr}{K_A} \quad (3)$$

Thus the horizontal distance between two inflexion points (and owing to almost identical shapes, between whole curves as well, excluding asymptotes) is :

$$D = \log \frac{k'r}{K'_A} - \log \frac{k''r}{K''_A} = \log \frac{K''_A \cdot k'}{K'_A \cdot k''} = \log \beta = \xi \quad (4)$$

or, expressing it in another way, the horizontal distance between a pair of R_F vs. f(pH) curves, when $k'r, k''r \gg 100$, is equal to the logarithm of the separation factor of the substances to be separated, as defined by Golumbic[4] ; or it is simply equal to the selectivity ξ (a term introduced by Kemula and Buchowski[5]) of the system with respect to the two substances, provided that $(H) \ll K_A$. Vice versa, an experimentally determined horizontal distance between two R_F vs. f(pH) curves gives directly log β for the solvent with respect to the two substances. This is illustrated in Fig. 2*a*, where a number of R_F vs. f(pH) curves is plotted ($kr \geqslant 100$) with different horizontal distances from the arbitrarily chosen reference curve 0. The relation (2) in this case simplifies considerably (by omitting the 1's from relations 1 and 2), becoming :

$$pH_{opt} = \frac{1}{2} \log \frac{k'r \cdot k''r}{K'_A \cdot K''_A} \quad (5)$$

The resulting error will not exceed 0·01 R_F, which lies within the experimental error of the method. Comparing (5) with (3), it can be easily seen that optimum pH value lies in the centre of the line connecting the pH_i values of a pair of components. In Fig. 2*b* the ΔR_F of different pairs of components at corresponding pH values are given.

Introducing pH_{opt} into ΔR_F (expression in brackets in formula 1, units omitted) we can calculate the maximum obtainable difference of R_F values between the two components considered :

$$\max \Delta R_F = \frac{\sqrt{\beta} - 1}{\sqrt{\beta} + 1} \quad (6)$$

Fig. 3 presents a plot of function (6), that is, it shows what maximum difference of R_F values may be obtained (at $pH_{opt.}$) with a given separation factor β, as defined by Golumbic[4]. At other pH values the differences of R_F are smaller. Thus formulæ 5 and 6 permit the theoretical prediction of the optimum pH value and the maximum resolution, expressed in terms of ΔR_F, from partition numbers and ionization constants of the substances which are being separated.

Since R_F vs. f(pH) curves for bases are mirror reflexions of those of acids (axis of symmetry at pH = 7), some of the relations deduced above must be altered if the substance under consideration is a base. Thus :

(1) $$\frac{d\Delta R_F}{dpH} = \frac{d}{dpH}\left(\frac{k'r/K'_B}{\frac{k'r+1}{K'_B} + 10^{14-pH}} - \frac{k''r/K''_B}{\frac{k''r+1}{K''_B} + 10^{14-pH}}\right) = 0$$

(2) $pH_{opt.}$ (base) = 14 − $pH_{opt.}$ (acid) ; K_A replaced by K_B.

(3) $$pH_i = 14 - \log \frac{kr}{K_B}$$

(4) unchanged, only K_A replaced by K_B

(5) $$pH_{opt.} = 14 - \frac{1}{2} \log \frac{k'r \cdot k''r}{K'_B \cdot K''_B}$$

(6) unchanged.

Figs. 1 and 2 can also be adapted to bases by replacing pH values by 14 − pH (as shown in Fig. 1).

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LETTERS TO THE EDITORS

RADIOPHYSICS

Radio Detection of the Planet Saturn

DETECTION of 3·45-cm. radiation from the planet Saturn has been accomplished with an X-band ruby maser radiometer[1,2] installed on the 85-ft. (26 m.) diameter, paraboloidal antenna at the University of Michigan's Radio Astronomy Observatory[3].

The initial detection on August 25–26, 1960, resulted from seven drift curves, one of which is shown in Fig. 1. The average of the seven drift curves indicates a peak antenna temperature of $0{\cdot}10 \pm 0{\cdot}028°$ K. Although the increase at the predicted position of the planet is visible on a single drift curve, the observation was repeated five days later to eliminate any possibility of confusion with radiation from other extra-terrestrial sources. At the time of the second observation, the predicted average change in Saturn's right ascension was 37·3 sec., westward; the measured average change was approximately 36·5 sec., westward. The average of the seven drift curves of the second observation indicates a peak antenna temperature of $0{\cdot}09 \pm 0{\cdot}028°$ K. These results are summarized in Fig. 2.

The total of fourteen drift curves, with a 'superimposed epoch' reduction technique, yields a peak antenna temperature of $0{\cdot}095 \pm 0{\cdot}02°$ K. This value indicates an equivalent black body disk temperature of $106 \pm 21°$ K., neglecting the effect of radiation from the rings. A correction factor of 2 per cent has been applied for terrestrial atmospheric absorption. This equivalent black body disk temperature is in reasonable agreement with that predicted from optical measurements[4].

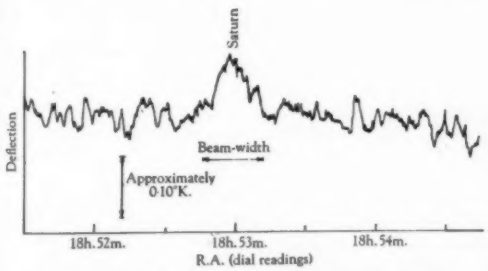

Fig. 1. Drift curve of the planet Saturn obtained with the maser radiometer: $\lambda = 3{\cdot}45$ cm. Peak antenna temperature is about 0·10° K.; integration time, 12 sec.

The peak antenna temperature of Saturn is about 350 times less than that measured from the standard source Cassiopeia *A* with the same system. In 1957, Drake and Ewen[5], using a 28-ft. antenna and a *TWT* radiometer at 3·75 cm., reported an antenna temperature for Saturn of 0·04° K. This reported detection was from one observation of 'off-on-off' type. This same paper reports an antenna temperature of 2° K. from Cassiopeia *A*. Their ratio of 50 could predict an antenna temperature of about 0·7° K. from Saturn, with the 85-ft. antenna of the University of Michigan, as opposed to our measured 0·10° K. The solid angle subtended by the planet during our measurements was the same as during the Drake and Ewen measurement of 1957.

The ruby maser radiometer developed by us is being described fully elsewhere[3]. Stated briefly, it is a modified Dicke system[4] with a switching input which is balanced off source on 'cold' sky. The maser preamplifier is a four-level ruby maser operating at 8·72 kMc./s. with push–pull magnetic field of approximately 4,000 gauss. The voltage-gain band-width product is typically 300 Mc./s., with a maser band-width of about 30 Mc./s. System band-width is at present intermediate-frequency limited at 8 Mc./s. The total equivalent system noise temperature is about 100° K., including antenna spill-over and back-lobes. These parameters result in a root mean square fluctuation of about 0·012° K. with a 12-sec. integration time. In Fig. 1 the root mean square fluctuation, taken as 1/4 the peak-to-peak off-source noise, is about 0·015° K. Thus the signal to peak-to-peak noise ratio for Saturn is about 2 to 1, on a single drift curve.

In this observation the modified Dicke system consisted of two identical horns pointed at the antenna surface, but physically separated so as to displace their beams by about 3·5 beam-widths in declination. Thus in all fourteen drift curves the comparison is between two discrete areas of the sky, one of which contains the planet. For small sources such as this, problems of balance and stability of gain are greatly reduced.

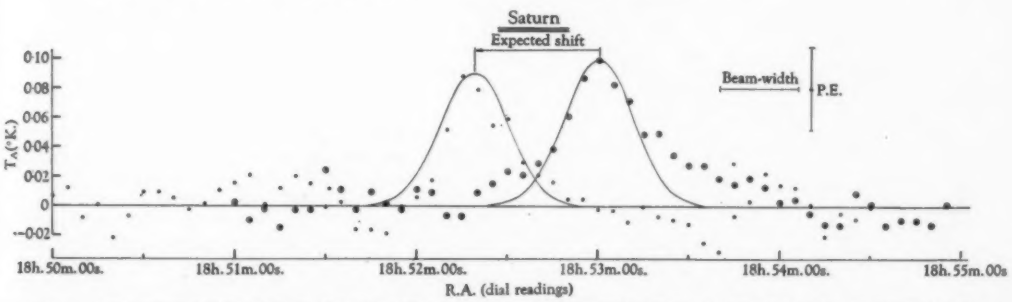

Fig. 2. Drift curves of planet Saturn, taken five days apart with the maser radiometer; ○, August 25–26; ●, August 30–31. Each is the average of seven individual drift curves. Solid lines are gaussian representation, at the expected shift of the planet

We are grateful to Prof. F. T. Haddock, A. H. Barrett, G. Makhov and W. E. Howard for their advice and support; to J. L. Talen, R. Yorks, R. W. Banta, F. Alred and W. Flowers for technical assistance.

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GEOPHYSICS

The Outer Radiation Belt and Auroræ

Rees and Reid[1] have found a diurnal variation in the latitude of the hydrogen lines in auroræ observed at College, Alaska. The variation is approximately sinusoidal with latitude minima at local midnight. They explain the phenomena by assuming that auroræ are produced by energetic protons and electrons which are sporadically scattered out of the outer radiation belt and showing that a day-side compression of the geomagnetic field by a continuous solar wind[2] could produce the latitude shift. The magnitude of the shift during geomagnetically quiet periods requires the solar wind to penetrate to within 4–5 Earth radii from the centre of the Earth. This corresponds to a translational kinetic energy density of about 300–600 keV./cm.^{3} for the wind, which is within the energy-range suggested by other measurements[3].

There is additional evidence which seems to corroborate this model. The position of the belt must have a diurnal variation such that the tips are always over the auroral regions at night and the day-side is slightly compressed from the usual dipole shape by the solar wind. The meagre space-probe observations of the belt[3–9] listed in Table 1 tend to

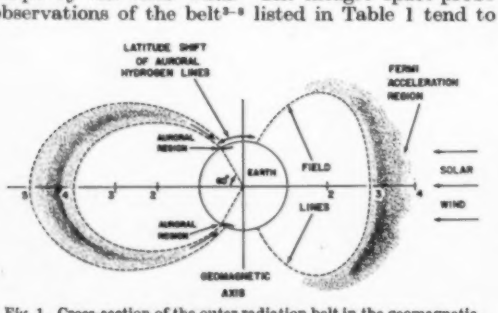

Fig. 1. Cross-section of the outer radiation belt in the geomagnetic meridian plane of the solar wind

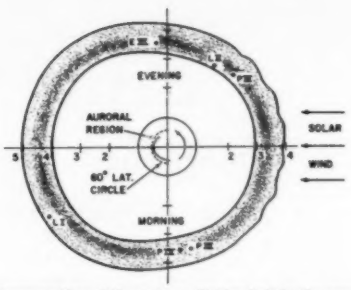

Fig. 2. Cross-section of the outer radiation belt in the geomagnetic equatorial plane. The labelled points are observed maxima listed in Table 1

support this unsymmetric model. In Table 1, φ is geomagnetic latitude; τ is local time; r is the geocentric radial distance in Earth radii; r_e is the radial distance of the dipole projection of r in the geomagnetic equatorial plane; and r_{ec} is r_e taking into account the day-side solar wind compression. Figs. 1 and 2 are schematic diagrams of the belt in meridian and geomagnetic equatorial planes. The seasonal variation of the direction of the solar wind and the difference between the geographical and geomagnetic axes have been omitted. In Fig. 2 the labelled points correspond to the space probe measurements listed in Table 1.

Table 1. Geomagnetic Co-ordinates of the Maximum of the Outer Radiation Belt

Space probe	Date	φ	τ	r	r_e	r_{ec}
Pioneer III (out, ref. 3)	Dec. 6, 1958	5° N.	0650	3·6	3·6	3·6
Pioneer III (in, ref. 3)	Dec. 7, 1958	15° S.	1510	3·3	3·6	3·4
Lunik I (refs. 4, 5)	Jan. 2, 1959	20° N.	0200*	4·2	4·8	4·8
Pioneer IV (ref. 6)	Mar. 3, 1959	0°	0630	3·6	3·6	3·6
Explorer VI (out, refs. 7, 8)	Aug. 9, 1959	7° N.	1820	3·6	3·6	3·6
Lunik II (ref. 5)	Sept. 12, 1959	33° N.	1600*	2·7	3·8	3·2

* The longitudinal logs of these trajectories are unavailable. The numbers were obtained assuming trajectories similar to that of *Pioneer* IV.

The agreement of the space-probe observations with the model may be fortuitous in view of the limited observations. However, all the probes listed in Table 1 passed through the region during geomagnetically quiet periods when *Explorer* VI has shown that the position of the outer belt is relatively stable. The theory could be tested by a single satellite in a highly eccentric orbit with a large rate of longitudinal precession.

Additional characteristics of auroræ might be explained with this model. The compression of the solar wind on the day-side will increase the magnetic field-strength and cause the mirror points of the trapped particles to be shifted nearer the geomagnetic equator. The day-to-night variation in the position of the tip of the belt shown in Fig. 1 was obtained assuming a 75 per cent increase in field-strength. This effect would prevent trapped particles in the belt from reaching auroral altitudes and explain the lack of day-time auroræ during geomagnetically quiet periods. The auroral $H\alpha$ profile maximum indicates that a large number of primary auroral protons have energies near 2 keV. (ref. 9), which is the same order of magnitude as the average solar wind proton energy. Parker[10] has shown how instabilities at the interface of the wind and the magnetic field result in Fermi acceleration of the particles (Fig. 1) and could pro-

duce the high-energy component of the auroral proton energy spectrum.

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PHYSICS

Observations of the Emission of Light on Dissolution of Irradiated Solids in Certain Liquids

Ahnström and Ehrenstein have observed the emission of light on dissolution of some organic solids in water[1]. We have been concerned with measurements of stored radiomimetic energy in solids treated with ionizing radiation. This problem has been approached partly by dissolution in liquids typical for dosimetry by the methods of radiation chemistry and partly by attempts to excite, during dissolution, liquid scintillators[2]. Some results of the latter kind will be summarized here. Most of the experiments were concerned with fine-grained sodium chloride which was given doses up to 200 Mrads of cobalt-60 γ-radiation and 2-MeV. electrons from a Van de Graaff machine.

Emission of light was observed by a photomultiplier (*EMI* 6255 *B*) and current recordings[3]. The solid is poured mechanically, using a manipulator, into a liquid contained in a quartz glass cup (Ekco's design for liquid scintillation counting). The liquid may be water, aqueous solutions, organic solvents or organic solutions.

It was noted that irradiated sodium chloride gave light pulses on dissolution in (aerated) water. The first part of the effect is very fast (rise-time about 0·5 sec.) and thus a fast recorder (Mingograf 230 *B* from the Elema-Schönander Co.) was selected. Emission of light was observed also for lithium fluoride, potassium iodide, glucose, saccharose and alginic acid. (The shape of the light-pulse of the latter was, however, flatter.)

Dissolution in the liquid scintillator described by Kallman and Furst[3] containing dioxane, diphenyloxazole, naphthalene and water gave less light than water itself, although it responds well to an external cæsium-137 source.

It was therefore decided to select solutes, known to be fluorescent to ultra-violet light or X-rays, that are either surface active, that is, exhibiting naturally a rather high concentration within the dissolution zone, or very slightly surface active, that is, having nearly the same concentration in the bulk solution and dissolution zone. Some simple inorganic ions approximate to the last case.

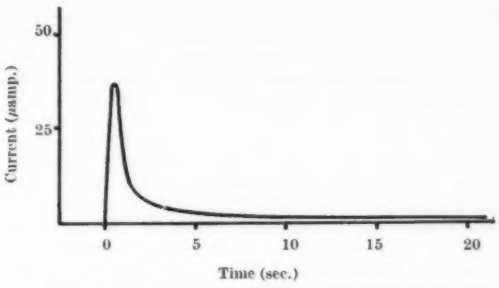

Fig. 1. Record of light emission on dissolution of 10 mgm. fine-grained sodium chloride (*pro analysi*) given a dose of 50 Mrads with 2-MeV. electrons 12 months before experiment (stored at + 4° C.). Solvent is $4{\cdot}2 \times 10^{-5}$ thallium chloride in water. The sodium chloride is dissolved within 1 min. The ordinate is anode current of the photomultiplier tube and well within its linear region. The system is quantitatively calibrated by tritium-water in the same apparatus

Following up these ideas, it was noted that a strong light emission is obtained with diphenyloxazole dissolved in water and with a commercial naphthalene sulphonic acid condensed with formaldehyde also in aqueous solution ('Belloid TD', a product of the Geigy Co.). Both systems should be regarded as surface active and the solutes as fluorescent. The total light output (found by measuring the total area of the light output pulse) was now nearly a thousand times greater than in the case of water. In a dark-room, the light flash occurring during dissolution is quite clearly seen. Fig. 1 shows a typical record in which the time-scale is also seen.

Similar experiments were performed with solutions of thallium chloride in water. This system is known to be fluorescent[4]. It seems to be somewhat surface-active. Here also, a large light output was observed —about a thousand times greater than that for water. Also this light flash is readily observed in the dark-room. It was found that the light output has a pronounced maximum at about 0·01 gm./litre thallium chloride.

A comparison with the luminescence of tritium water (~100 mc./ml.) containing thallium chloride was made. This solution exhibited a small but easily measurable fluorescence. Assuming that the stored energy acts like radiation and excites the thallium ion electronically, we found that, using 0·01 gm./litre thallium chloride, the energy stored was about $1{\cdot}5 \times 10^{8}$ ergs/gm. or 3 per cent of the primary absorbed dose. This figure is of the same order as that found by using chloroform as a detector[2].

It was further observed that irradiated alginic acid gave a light-pulse; but, after storage in humid air (98 per cent relative humidity, 20° C.) for one day, no light emission was observed.

Irradiated polystyrene samples gave rise to luminescence when dissolved in the liquid scintillator *NE* 213 (xylene, *POPOP*, from Nuclear Enterprises, Ltd.). Samples treated by electrical a.c.-corona discharges (by Dr. A. Kelén, ASEA Co.) gave similar light pulses, thus yielding a qualitative indication of the equivalence between the action of ionizing radiation and electrical discharges.

Further observations showed that lanthanide ions known to be fluorescent, namely, gadolinium, neodymium, samarium, terbium and europium, did not amplify the water light-pulse for sodium chloride. It is not clear at present why the lanthanide ions do

not give large luminescence effects whereas thallium ions and organic fluorescent solutes do.

These results might be of some significance for health problems which may eventually be encountered in food preservation by irradiation[1,2]. They show that dry substances store energy but that hydrophilic materials lose this energy on sorption of water. No strict proof of radiation-equivalence is obtained because the average wave-length emitted is around 4000 Å. Nevertheless, the results indicate that the phenomenon of stored energy has to be carefully examined, at least for dry solids, before preservation of food by irradiation is adopted on a large scale. For further details, see ref. 2 and a more complete paper given elsewhere. The work on ionic crystals has some relation to the discussion of stored energy and volcanism[5].

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Aberration of Plane Waves

By 'aberration' is meant the change in the apparent angular position of a source (usually at infinity) due to a change in the velocity of the observer.

In elementary treatments of this phenomenon, the source is considered as a source of particles and the required formula is obtained by applying the rules for addition of velocities. It will be shown here that the result obtained in this simple way is also valid for plane waves with velocity c, but is not valid for plane waves having other velocities. For example, the aberration of sound in Newtonian mechanics is zero, whereas a misapplication of the addition of velocities rule would lead one to think that there should be an aberration of the order of the change in velocity of the observer divided by the velocity of sound.

The fact that there is no classical aberration for sound may be realized by thinking of the following experiment:

A sound-direction finder or sound telescope is made from several small microphones attached to a rigid structure so that they are coplanar; the signals from the microphones are received without appreciable delay by an integrating apparatus which is also part of the rigid structure. When this telescope is activated by the sound from a far distant source, the total signal received is maximum when the signals from the individual microphones are in phase, that is, when the plane of the microphones is parallel to the planes of the oncoming waves. If a change in velocity is now imposed on the telescope, it is clear that the above condition of parallelism will not be destroyed. Hence, no re-orientation of the telescope for maximum signal is necessary, which means that there is no aberration.

Consider two observers O and O' moving with respect to one another, so that O sees O' moving with velocity v in the positive direction of their common x-axis. Let the y and z axes of O be parallel respectively to those of O'. The Lorentz transformations which relate the measurements of these observers are:

$$x = \gamma(x' + vt') \; ; \; y = y' \; ; \; z = z'$$

$$t = \gamma\left(t' + \frac{vx'}{c^2}\right), \text{ where } \gamma = 1/\sqrt{1 - v^2/c^2}$$

Suppose O observes the plane wave:

$$\chi = \exp 2\pi i\left(\frac{lx + my + nz}{\lambda} - ft\right)$$

that is, he observes it as moving in the direction (l, m, n) with velocity $f\lambda$.

The manner in which O' observes the same wave can be obtained by substituting for x, y, z and t in terms of x', y', z', and t' giving:

$$\chi = \exp 2\pi i\left(\frac{l'x' + m'y' + n'z'}{\lambda'} - f't'\right)$$

where $\dfrac{l'}{\lambda'} = \dfrac{\gamma(l - vf\lambda/c^2)}{\lambda}$

$$\frac{m'}{\lambda'} = \frac{m}{\lambda} \; ; \; \frac{n'}{\lambda'} = \frac{n}{\lambda}$$

$$f' = \gamma\left(f - \frac{lv}{\lambda}\right) = \gamma\left(1 - \frac{lv}{f\lambda}\right)f$$

From these equations one obtains the general aberration formula:

$$l' : m' : n' = \gamma\left(l - \frac{vf\lambda}{c^2}\right) : m : n$$

A common case of aberration is when the oncoming wave is moving roughly at right angles to the relative velocity of the two observers. Let its direction of motion as observed by O be in the direction of the negative y axis, that is: $(l, m, n) = (0, -1, 0)$.

The direction of motion as observed by O' will differ from that of the negative y axis by an angle θ where $\tan\theta = \dfrac{l'}{m'}$. From the general formula above it is evident that:

$$\tan\theta = \gamma\frac{vf\lambda}{c^2}$$

This formula becomes the usual one $\left[\tan\theta = \dfrac{v}{c}\right]$ for the case of astronomical aberration. It also explains why the aberration of waves vanishes in non-relativistic mechanics, that is, as $c \to \infty$.

Even though the apparent direction of a distant sound source does not depend on the motion of the observer it does, nevertheless, vary with the velocity of the medium relative to the source. This effect may be understood classically as follows:

When a signal is emitted by the source, it progresses as a spherical wave the radius of which grows with the velocity of sound and the centre of which remains fixed in the medium (that is, moves with the wind). The sound telescope of any observer (regardless of his velocity) at a point P must for maximum signal be aimed at the position of the centres of the waves as they pass P. From this it follows that, if $\mathbf{s}$ is the unit vector in the direction of the sound telescope at

maximum signal and V the velocity of sound in still air and **w** the velocity of the wind with respect to the source, the vector $V\mathbf{s} - \mathbf{w}$ points in the true direction of the source.

This latter phenomenon should not be treated as aberration because it is not associated with the motion of the observer, and because the direction of the effect is opposite to what one gets from the over-simplified application of the law of addition of velocities referred to at the start of this paper.

I wish to express my thanks to Prof. J. L. Synge for a very stimulating discussion on this topic.

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Forces on Charged Particles of a Plasma in a Cavity Resonator

Following the methods adopted by Boot *et al.*[1], we have recently undertaken an analysis of the conditions required for the containment of an ionized plasma by electromagnetic waves at high frequency, taking collisions and space-charge forces in the plasma into account. During this work, now being prepared for publication, one of us (H. G.) directed attention to the fact that two types of confining force are present when the plasma interacts with the wave in the presence of large field gradients. One is due to the electric, or induced electric, field acting directly on the electrons, as analysed by Boot *et al.* For this force to be unidirectional, certain relations between amplitude, gradient and frequency of the electric field and electron density must be fulfilled. We call this the Mathieu force, since these relations may be obtained by examining the differential equation which is of the Mathieu type[2]. The other unidirectional force we call the electromagnetic force. This force results from the interaction of the electron current set up by the electron moving in the electric field with the magnetic field component of the electromagnetic wave. This is the force considered by Volkov[3].

The nature of the solution of the Mathieu equation may be deduced from an examination of the stability chart (Fig. 1). The operating point (a, q) appropriate to a particular region of the plasma is dependent on the plasma parameters, the generator frequency, and the square of the electric field gradient $(\mathrm{d}E_0)/(\mathrm{d}x)^2$. For a cylindrical cavity excited in the TM_{010} mode:

$$a = \frac{\omega_p^2}{\omega^2} - \frac{2{\cdot}75e^2}{m_e^2c^2}\cdot(\omega^2 - \omega_p^2)\times$$

$$\frac{2\omega_p^4 - 3\omega^2\omega_p^2 + \omega^4 + \omega^2\nu^2}{\{\omega^2\nu^2 + (\omega^2 - \omega_p^2)^2\}^{3/2}}\left(\frac{dE_0}{\mathrm{d}x}\right)^2 - \left(\frac{\nu}{2\omega}\right)^2$$

$$q = \frac{1{\cdot}375\ e^2}{m_e^2c^2}\cdot\frac{2\omega_p^4 - 3\omega^2\omega_p^2 + \omega^4 + \omega^2\nu^2}{\{\omega^2\nu^2 + (\omega^2 - \omega_p^2)^2\}^2}\left(\frac{\mathrm{d}E_0}{\mathrm{d}x}\right)^2$$

where ω_p is $2\pi\left\{\frac{ne^2}{\pi m_e}\right\}^{1/2}$; ν is the collision frequency for momentum transfer between electrons and atoms or ions; $\omega/2\pi$ is the generator frequency; and E_0 is the electric field in the cavity.

Solutions for points (a,q) which lie below a_0 or between a_2 and b_2, etc., correspond to a unidirectional force on the electrons. Those for points which lie between a_1 and b_1, a_3 and b_3, etc., correspond to exponentially increasing amplitudes of oscillation of the electrons. Although this latter condition is not effective for containment, yet, if collisions between atoms and electrons are appreciable in number, it will result in conversion of the radio-frequency energy into plasma heating.

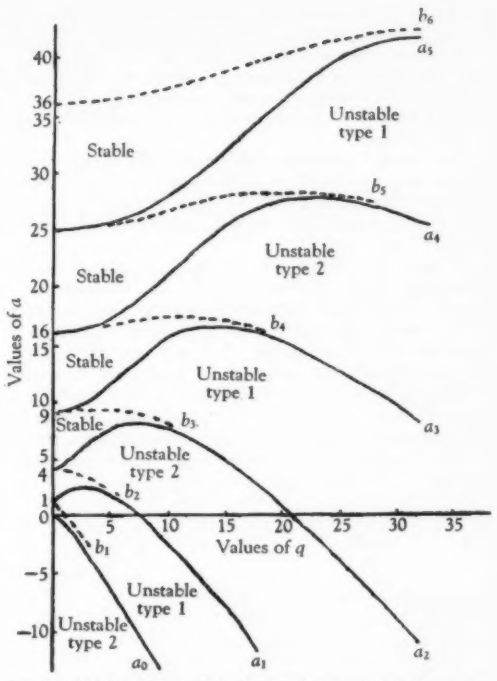

Fig. 1. Stability chart. This diagram is symmetrical about the a-axis

The Mathieu force and the electromagnetic force both originate from the electric field gradient, although for different reasons, and this makes it difficult to separate them mathematically. However, the role of the Mathieu force may be illustrated by putting $\omega = \omega_p$, when the electromagnetic force disappears.

In general, it may be said that, in the region below a_0 in Fig. 1, the electromagnetic force predominates, while between a_2 and b_2 the Mathieu force predominates; but it should be noted that this is not always true, and the electromagnetic force may oppose confinement for certain values of plasma parameters. It can be shown that concentration of the ionized portion of a partially ionized gas is also feasible. The relevance of this to the experiments of Self and Boot[4] has not yet been examined in detail, but they would appear to support our conclusions.

In practice, under the most general plasma conditions, it seems unlikely that containment of a fully ionized plasma will be obtained by operating in the (a_2b_2) region where the Mathieu force predominates, partly due to the large field gradients required, and partly due to the difficulty in obtaining the correct relative values for a and q. Our analysis does show, however, that when the special conditions of plasma resonance as defined by Dutt and Stainsby[5] are satisfied, and when $\nu \ll \omega_p$, the operating point (a,q) can lie between a_2 and b_2 for moderate input

powers, resulting in a unidirectional Mathieu force on the plasma of appreciable magnitude.

Since completing this analysis we have seen a letter from C. M. Haaland[6] in which he distinguishes between the Mathieu and electromagnetic forces; but seems not to have noticed the phase-dependence of the latter.

The forces considered above are additional to those due to the pinch effect, considered by N. J. Phillips (private communication) for high-frequency currents, which will be present at the surface of a contained plasma.

It may be of interest to note that our analysis resembles that of Prof. W. K. R. Watson[7] in his theory of fire-ball formation, except that he apparently omits the space-charge terms and does not consider the electromagnetic force as defined by us. His statement that the charge tends to concentrate at the voltage nodes is supported by the analysis and experiments of Boot *et al.*, Volkov's analysis, the experiments of Glagolev *et al.*[8], and our own analysis.

Our thanks are due to Mr. J. K. Brown, director of research, for permission to publish this communication.

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A New Micrometer Microscope

The usual method of measuring the dimensions of microscopic objects is to compare them against an eye-piece scale or to use a calibrated filar micrometer eye-piece. Such methods are not capable of great accuracy and are inherently slow and poorly adapted to statistical problems. In order to plot the size distribution of a large number of particles, it is necessary to bring each in turn to the centre of the field and to set it against the scale.

These difficulties can be avoided by means of a double-image system in which two images, sheared by a controlled amount, are viewed. If the separation of the two images of a particle is less than its diameter, they will overlap. If the separation is greater than the diameter, a clear space will be seen between them, and if the separation is equal to the diameter they will just touch. The position of contact can be observed with great precision, and theoretical calculations by J. Dyson (unpublished work) have shown that the accuracy of setting may be considerably better than the resolving power.

Only two double-image micrometer microscopes appear to have been described. McGinn[1] used birefringent elements which introduced some aberration and gave only a small amount of shear. Timbrell[2] used a mirror vibrating at 50 c./s. phased with an interrupted light source. The shear was controlled by varying the amplitude of vibration of the mirror. This system requires relatively complicated electrical accessories and cannot readily be used with any type of microscope. A purely optical instrument similar to the Mach-Zehnder interferometer has been constructed in the workshop of this Department by Mr. A. B. Charters and is shown diagrammatically in Fig. 1. P_1 and P_2 are two beam-splitting prisms; M_1 and M_2 are two surface-metallized mirrors. The instrument is constructed as an attachable body that fits just above the objective carrier. M_2 can be rotated through a small angle by means of a differential screw micrometer mechanism, producing a sheared image in one azimuth. Shears equal to the diameter of the entire field of view can be obtained at any power. The direction of shear can be altered by rotating the whole attachment about the optical axis of the microscope; an angular scale is provided. It is thus possible to plot the shape and dimensions of an irregular object in polar co-ordinates.

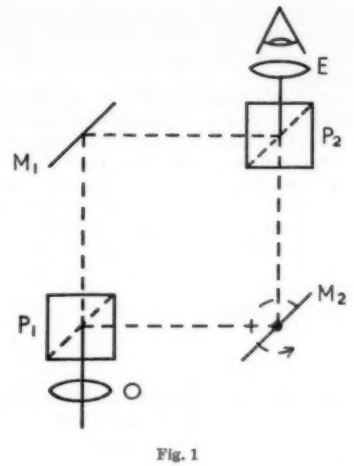

Fig. 1

A special advantage of this system is its use for plotting statistical size-distribution curves. For this purpose the micrometer is set at a known value. On observing the field of particles, those with diameters greater than this value will give overlapping images, those with diameters less than this value will give two separated images and a few may give images that just touch. The number in each category can easily be determined. The micrometer is then set to another value and the process is repeated. In this way an integrated distribution curve can be obtained without making an actual measurement on a single particle. The instrument can be used with almost any method of microscopy, including phase contrast, and it can be readily applied to living cells, including motile ones.

Many modifications of the basic system are possible. Colour filters can be inserted into one or both paths and are sometimes helpful in distinguishing the sheared from the unsheared image. The three elements, P_1, P_2 and M_1, could be incorporated into a single solid block of glass. A modified version in the form of a convenient eye-piece attachment with a different mechanical system, but giving a smaller

total shear, has been designed by Dyson (unpublished work).

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METALLURGY

Hydrogen Diffusion in Mild Steels

Despite evidence in the literature that hydrogen diffusion in steels does not obey Fick's laws, experimental data continue to be analysed in their terms. A further deviation from these laws is presented here, and its relation to Fick's laws are discussed. An explicit statement of the inapplicability of Fick's laws to hydrogen in steels, at least below 100°, is desirable.

The solution of Fick's laws for the evolution of a diffusing species from a cylinder of radius a, length l in which the species is at uniform concentration at time $t = 0$ and the surface concentration is zero for $t > 0$ is given[1] by :

$$\frac{Q}{Q_0} = \left[4\sum_1^\infty \frac{1}{\beta_n^2} \exp\left(-\frac{\beta_n^2 Dt}{a^2}\right)\right] \left[\frac{8}{\pi^2}\sum_1^\infty \frac{1}{(2m-1)^2} \exp\left(-\frac{(2m-1)^2\pi^2 Dt}{l^2}\right)\right] \quad (1)$$

where Q and Q_0 are the total quantities of the species in the cylinder at times t and zero respectively, β_n is the nth root of the equation $J_0(X) = 0$, and D is the diffusion constant. After a comparatively short time, the first term in the series in the left-hand bracket becomes dominant, and the practice[2-5] is to assume that after $\frac{Q}{Q_0}$ is less than approximately 0·5, the equation followed is :

$$\frac{Q}{Q_0} = \frac{32}{\pi^2\beta_1^2} \exp\left[-\left(\frac{\beta_1^2}{a^2} + \frac{\pi^2}{l^2}\right)Dt\right] \quad (2)$$

If the evolution of hydrogen from a steel cylinder is measured by following the increase in pressure in a constant volume apparatus with time,

$$\frac{Q}{Q_0} = 1 - \frac{p}{p_f} \quad (3)$$

where p and p_f are the pressures at time t and infinity respectively and $p = 0$ at $t = 0$.

Hence after an initial period, from equations (2) and (3) :

$$y = \frac{32p_f}{\pi^2\beta_1^2} \exp(-Kt) \quad (4)$$

$$\frac{dy}{dt} = -\frac{32Kp_f}{\pi^2\beta_1^2} \exp(-Kt) \quad (5)$$

where $y = p_f - p$ and $K = \left(\frac{\beta_1^2}{a^2} + \frac{\pi^2}{l^2}\right)D$

Hence if Fick's laws are obeyed, plots of both log y and log $\left(\frac{dy}{dt}\right)$ against t should yield, after an initial period, straight lines of slope $-K$ from which D can be obtained.

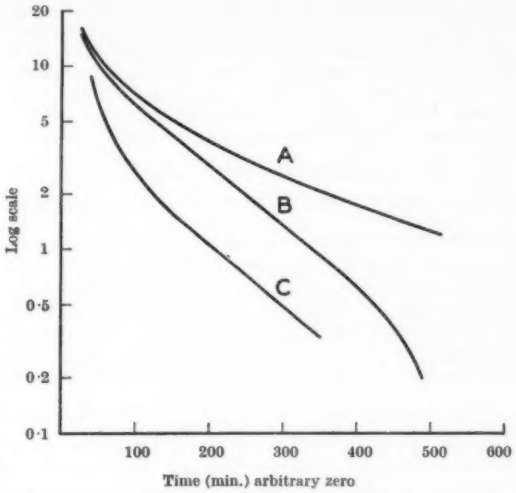

Fig. 1. Evolution results for ½-in. diameter cylinder. *A*, log y versus t. *B*, log $(y - y_1)$ versus t. *C*, log $\left(\frac{dy}{dt}\right)$ versus t

Evolution experiments have been carried out on mild steel cylinders, 4 in. long and with nominal diameters of ½ in., $\frac{7}{16}$ in. and ¾ in., which were saturated with hydrogen by immersion in 3 per cent sodium chloride solution saturated with hydrogen sulphide at 25°. Hydrogen evolutions at 65° C. were studied by following changes in pressure in an initially evacuated constant volume gas burette with a mercury manometer until constant pressure was attained. In each case, values of y were calculated, and values of $\frac{dy}{dt}$ were obtained graphically from plots of y versus t.

The results for a ½-in. diameter cylinder are given as semi-logarithmic plots in Fig. 1. Curve *C*, displaced vertically for clarity, shows that equation (5) is obeyed to the extent of giving, after an initial period, a line which is straight within experimental error throughout the range in which slopes could be determined graphically. Curve *A*, however, has curvature over its length and thus shows that equation (4) is not obeyed. This length corresponds to the evolution of 90–95 per cent of the total. Indications so far are that the evolution thereafter is exponential.

It is necessary to show that the results reported here are a measure of the movement of the hydrogen within the steel and not a measure of any surface processes. This can be done by using specimens of different dimensions, and showing that some measured property of the system is a function of the specimen volume, and not of the specimen surface area[6]. The slope of the log $\left(\frac{dy}{dt}\right)$ versus t plot was found to be a reproducible property and could be characterized by $t_{1/2}$, the time required for log $\left(\frac{dy}{dt}\right)$ to halve its value. $t_{1/2}$ was determined using cylinders of different radius (a) and Table 1 shows that $t_{1/2}$ varies as a^2 as required.

Table 1

a^2 (in.^{2})	0·0622	0·0475	0·0350
$t_{1/2}$ (min.)	155	113	90
$10^2 a^2/t_{1/2}$	4·0	4·2	3·9

The behaviour of curves A and C is due to the fact that y decays exponentially within experimental error over a limited range; but this decay requires a finite value of y at infinite time, that is, the relation $y - y_1 = A \exp(-Bt)$, where y_1, A and B are constants, holds during a substantial portion of the evolution. Thus within this range of applicability, $\log\left(\frac{dy}{dt}\right)$ versus t is linear, but $\log y$ versus t is not. Curve B shows that y_1 can be chosen to give a linear plot of $\log(y - y_1)$ versus t with the same slope as $\log\left(\frac{dy}{dt}\right)$ versus t. Curve B shows the deviation from the linear relation at large values of t, when y is approaching y_1 in value. It follows that curve C would show deviations over the same range but with opposite curvature to curve B. Direct measurement of this was precluded by the sensitivity of the apparatus used.

This deviation in a plot of $\log\left(\frac{dy}{dt}\right)$ versus t has been reported previously for evolutions at higher temperatures[2], and attributed to the appearance of "residual or slowly-diffusing hydrogen . . . a real component or effect detectable only after the removal of the rapidly diffusing or 'diffusible' hydrogen".

Now for valid diffusion constants to be obtained for a given system, it is essential that all equations derived from Fick's laws be obeyed. There are already important experimental data obtained below 100° which do not obey the appropriate equations derived from Fick's laws[7,8]. The division of the hydrogen in solution into 'diffusible' and 'residual' fractions in the present case would therefore be based on deviations from an equation which would not be expected to apply.

The present results provide more evidence against the applicability of Fick's laws and additional data to be explained by a comprehensive theory of the behaviour of hydrogen in steels.

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Crucible Material for the Growth of Palladium Single Crystals

Investigations in this laboratory of the catalytic activity of palladium indicated that it was desirable, during a particular measurement, to limit the active surface to a single crystallographic plane. For such experiments large single crystals of palladium were required. This resulted in the development of a crystal-growing apparatus (to be described elsewhere) in which the Bridgman[1] method was utilized, and in an investigation of crucible materials suitable for containing molten palladium. The results of this latter work are reported here.

Although metals of the platinum group are quite inert under most conditions, they react with many common substances when molten. The molten platinum metals will dissolve appreciable quantities of carbon, most of which will be rejected as graphite on slow cooling. Palladium and silicon form the compounds Pd_3Si and PdSi (ref. 2). Palladium and Pd_3Si form a eutectic mixture at 6 per cent silicon, melting at 670° C. Aluminium oxide has been reported to be stable in contact with molten nickel at 1,800° C. in an inert atmosphere[3]. From the foregoing considerations, pure aluminium oxide was selected as the crucible material (E. M. Wise, International Nickel Co., states in a private communication that he has used aluminium oxide for containing palladium melts). A crucible of morganite (99·7 per cent aluminium oxide), 8 mm. internal diameter, 12 mm. external diameter, 8 cm. long with a rounded, closed end was used.

Fig. 1. Palladium ingot—side view

The crystals were grown by the following technique. Chemically pure-grade palladium moss was compressed in a steel die to small pellets slightly less than 8 mm. in diameter. Approximately 25 gm. of palladium pellets were inserted in the crucible and the crucible placed in the crystal-growing apparatus. This was flushed with argon at room temperature and again at 500° C. The final argon pressure was 3 lb./sq. in. gauge. The palladium was brought to 1,650° C., approximately 95° above its melting point. The crystals were grown at a dropping rate of 3 cm. per hr. No attempt was made to determine the optimum growing-rate.

Crystals 8 mm. × 40 mm. were easily grown under these conditions. A typical ingot is shown in Fig. 1. Except for a 3-mm. region at the top, the entire ingot is a single crystal. The small zone at the top consists of four small crystals of different orientation (Fig. 2). The orientation of the crystal axes of the large crystal with respect to the direction of growth was determined by Laue back-reflexion photographs: a cube edge forms an angle at about 20° with the axis of the ingot.

Liquid palladium does not wet aluminium oxide, and any gas entrapped in the melt tends to adhere to the crucible walls. This gas is difficult to remove. Even when the pressure is reduced to the point where a considerable amount of palladium distils to the cooler parts of the furnace, small surface bubbles occur on the palladium ingot. The surface bubbles which formed at the molten palladium–aluminium oxide interface are clearly visible in Fig. 1.

Aluminium oxide is satisfactory from the point of view of purity. No evidence of reaction between the crucible and molten palladium was found. Spectroscopic analysis indicated 100 p.p.m. of silicon and iron in the crystal—no more than in the starting material.

The results of this investigation show that pure aluminium oxide is satisfactory as a crucible for molten palladium. As no reaction is detectable between the crucible and the melt, the finished crystal can easily be removed from the crucible

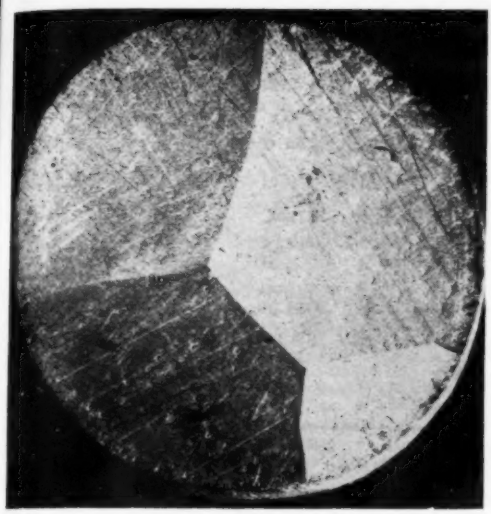

Fig. 2. Palladium ingot—top view

because the melt does not wet its container. When aluminium oxide is used as the container in growing palladium crystals, the diameter of the single crystal ingot should exceed the diameter of the crystal desired because of the gas bubbles, which collect at the crystal-container interface.

This investigation has been supported in part by International Nickel Company, Inc., New York.

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CHEMISTRY

A Photoionization Detector for Gases and Vapours

Sensitive ionization methods for the measurement of low gas and vapour concentration require the ionization of the test gas or vapour under conditions where an inert carrier gas is unionized. Such methods as the ionization of carbon compounds in a hydrogen flame[1] and the reaction between gases and vapours and rare gas metastables[2] are well established and successful for this purpose. An alternative method is to irradiate the gas mixture with ultra-violet radiation of such a frequency that photoionization of the test gas occurs without any accompanying ionization of an inert carrier gas. In practice an electrical discharge in one of the rare gases or in nitrogen or hydrogen generates photons of energy sufficient for the ionization of almost all polyatomic compounds, but with insufficient energy to ionize simple diatomic gases.

A practical photoionization detector is illustrated in Fig. 1, together with the details of its construction. The gas supply to the discharge which generates the ultra-violet radiation is led through the tube (*A*); this tube also serves as a cathode for the discharge, and in use a current of a few m. amp. is maintained between this cathode and the anode (*B*). The test gas is introduced through the tube (*D*); this also serves as the collecting electrode for the ions liberated within the chamber enclosed by the second cathode (*C*). When the discharge is supplied with hydrogen, nitrogen or argon it is necessary to reduce the pressure within the detector to 100 mm. or less; at higher pressures a stable discharge is difficult to maintain. With helium however a stable discharge is possible at atmospheric pressure particularly if the detector is supplied with radiofrequency energy instead of d.c.[3]. The carrier gas in which the test sample is introduced into the sensing chamber (*C*) can be almost any gas which is not itself ionized by the radiation from the discharge. Water-saturated air, for example, gives entirely satisfactory results.

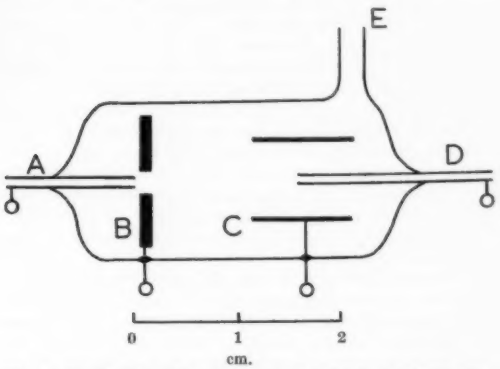

Fig. 1. Construction of the detector. *A*, Inlet for discharge gas and cathode connexion; *B*, discharge anode; *C*, measuring chamber anode; *D*, sample inlet and cathode; *E*, outlet to water pump. The detector body is of glass, the cathodes of platinum tubing and the anodes are of copper

The detector illustrated gave a current of approximately 10^{-10} amp. in the absence of ionizable vapour, possibly due to the photoelectric emission of electrons from the surfaces of the measuring chamber (*C*). In the presence of ionizable vapour, a substantially linear response to vapour concentration was observed up to a signal current of 10^{-7} amp. The efficiency of ionization of propane as a test substance was approximately 0·01 per cent. The response of the detector appeared to be unaffected by gross contamination of its surfaces with dirt or decomposition products and was stable over long periods and on repeated operation. The stability of this device, unlike that of other discharge methods of measuring vapour concentration, is probably due to the fact that the discharge takes place within the hollow cathode (*A*), which contains only a clean and uncontaminated supply of inert gas. The design shown should not be considered as final, but rather to illustrate the potentialities of this method.

I am indebted to Mr. P. Simmonds for technical assistance.

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Absorption Spectra of Copper(II) and Nickel(II) Complexes

It has been demonstrated that there is a definite relation between the basicity of ligands and the stability of the complexes[1-3]. There are, however, few data in the literature dealing with the relation between these two factors and the absorption spectra; as an example may be mentioned the work of Jones *et al.*[4].

It is known[5] that the bands appearing in the absorption spectrum of the electrovalent, normally paramagnetic copper(II) and nickel(II)-complexes, belong to the transition $^3E_g \rightarrow {}^3T_{2g}$ and $^3A_{2g} \rightarrow {}^3T_{2g}$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)$, $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ respectively. If the distance between the sub-levels, due to the effect of the electrostatic field of the ligands, increases, then the bands corresponding to these transitions appear shifted to shorter wave-lengths. The polarization of the ligands plays an important part in the formation of the electrostatic field[6]. The short-wave shift observed with the different ligands means increase of the field and simultaneously that of the polarization[7]. The increase of the covalent character of the bonds results also in a shift of similar direction; and further, the intensity of the bands increases with the σ-donor properties of the ligands[8].

Our experimental results show that the intensity of the bands in the copper(II) complexes increases in the order ammonia–ethylenediamine–1,2 propylenediamine – trimethylenediamine – triethylenetriamine – tetraethylenepentamine (see, for example, ref. 8), whereas in nickel(II) complexes the order is ethylenediamine–ammonia – trimethylenediamine – tetramethylenepentamine–triethylenetriamine. The extinction value of the bands in general increases with the length of the polyamine chain (trimethylenediamine–triethylenetriamine–tetraethylenepentamine) and with the increase of the size of the chelate rings produced (see Table 1).

In copper(II) complexes there are increases not only in the intensity but also in the width and splitting of the bands with the length of the polyamine chain[9]. The change of the extinction value of the bands is not so regular in the case of nickel(II) as in that of copper(II). The λ(water)/λ(complex) values (that is, the shift in relation to the hydrated ions) compared with the log β_n values, in both the copper(II) and nickel(II) complexes, is in good agreement with a linear relationship (Fig. 1).

In the case of the nickel(II) complexes, the distance between the red band and blue band is considerably changed ($\lambda_{II}-\lambda_{III}$; $\Delta\lambda$). As the stability increases, these bands get nearer to each other, indicating the approach of the terms $^3T_{1g}(F)$ and $^3T_{1g}(P)$. The λ_{II} and $\Delta\lambda$ values give a straight line in good agreement (Fig. 2). The log β_n and λ(water)/λ(complex) values change in almost the same way in the case of both metal ions.

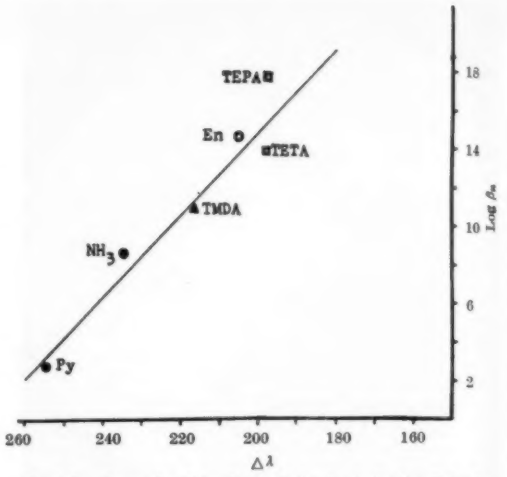

Fig. 1. Log β_n as a function of $\Delta\lambda$. ●, log β_6; ▲, log β_3; ○, log β_2; □, log β_1

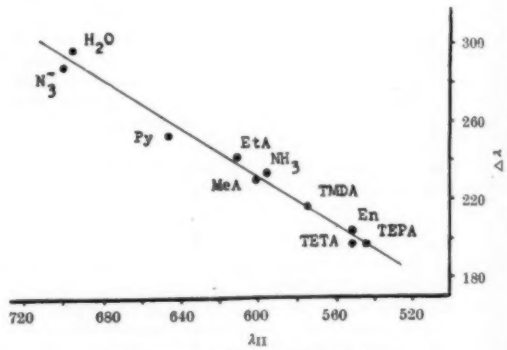

Fig. 2. A plot of $\Delta\lambda$ against λ_{II} (Ni)

According to the D_q values in the nickel(II) complexes the order may be as follows:

$$NO_2^- > NO_3^- > N_3^- > H_2O = Py > NH_3 = EtA > MeA > TMDA > TEPA > TETA > En$$

Table 1

Ligand	mμ and log ε Ni(II)			Cu(II)		Ligand	Ni(II)			Cu(II)	
H_2O	1,150	695	395	792	—	MeA	1,000	600	368	—	—
	0·24	0·28	0·68	1·12			0·72	0·90	1·11		
NO_2^-	1,175	700	383	754	—	TMDA	930	574	357	574	—
	0·30	0·27	0·91	1·61			0·66	0·79	0·93	2·01	—
NO_3^-	1,170	710	397	820	—	DETA	—	—	—	710	—
	0·28	0·26	0·66	1·09	—					2·01	
N_3^-	1,160	700	410	750	—	En	890	550	345	555	—
	0·99	0·94	1·48	2·23			0·79	0·71	0·89	1·69	—
Py*	1,150	645	390	688	—	TETA	920	550	352	850	587
	0·47	0·75	1·07	2·22			1·01	0·86	1·10	1·30	2·12
NH_3	1,010	595	360	605	—	TEPA	922	545	347	860	656
	0·56	0·76	0·94	1·68			1·10	0·82	1·30	2·00	2·22
EtA	1,010	610	368	—	—	1,2-Pn	—	—	—	540	—
	0·72	0·90	1·10							1·80	

* Py, Pyridine; EtA, ethylamine; MeA, methylamine; TMDA, trimethylenediamine; DETA, diethylenetriamine; En, ethylenediamine; TETA, triethylenetetramine; TEPA, tetraethylenepentamine, 1,2-Pn, 1,2-propylenediamine.

while the order of stability[10] is :

$$Py < NH_3 < TMDA < TEPA < En$$

In the copper(II) complexes :

$$NO_3^- > H_2O > NO_2^- > N_3^- > Py > TEPA > NH_3 > TETA > TMDA > En > 1,2\text{-}Pn$$

which differs slightly from the stability order.

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A Technique for pyrolysing or vaporizing Samples for Gas Chromatographic Analysis

A TECHNIQUE was recently reported where rapid heating by induction was used to sublime solid inorganic, organic, and metal complexes[1]. The fine powdered sublimate was collected on salt plates and infra-red spectra were determined. The results indicated that very small particle size was obtained, as well as very little decomposition even for organic compounds, although the sublimation technique consisted of heating a platinum dish containing the compound from room temperature to white heat in a few seconds.

It occurred to us that the gaseous products of such a sublimation could be introduced into a gas chromatograph and thus separated for further study.

Normally, a fixed-temperature vaporization block is used on gas chromatographs, so that all possible gaseous products are produced instantaneously ; however, it is difficult to choose a temperature which is satisfactory for all components. It was hoped that the rapid heating by induction would result in a series of gaseous products being produced as the temperature rose, each vaporizing at an optimum temperature. Since the time required to reach very high temperatures is only a few seconds, each component would be introduced into the vapour state almost instantaneously, and no broadening of peaks should be seen on the chromatograph.

Two advantages were sought for. First, some separation of volatile from less-volatile components should take place by virtue of the slight time required to pass from low to high temperatures ; second, the possibility of reducing cracking of materials unstable at high temperatures, since they will volatilize before cracking temperatures are reached. It should also be possible to use this heating technique for vaporizing viscous or high-boiling liquids which cannot be handled by the usual chromatographic techniques. Pyrolysis of polymers can also be done, since extremely high temperatures can be reached. We have concentrated on this latter work at present and would like to report the results. Some results concerning the other advantages listed were obtained during the work on polymers.

A chromatographic instrument of our own design[2] was modified so that one loop of a gas valve passed through the induction coil of a Leco model *IH*-15 furnace. In our instrument it is possible to make this loop part of the column-detector circuit, or place it under vacuum, or make it part of a loop not entering the instrument. Using the first loop it is possible first to pyrolyse a polymer in a vacuum and then introduce the resulting gases into the column-detector circuit. The second loop can be used to pyrolyse while the helium-flow brings the gases through the column-detector circuit. By comparing chromatographs obtained by both techniques, it is possible to see if better separation of components is obtained by rapidly changing the temperature of the sublimation apparatus or by holding it constant. We are assuming here that the technique of pyrolysing into a helium stream gives chromatographs indicative of a changing temperature sublimation apparatus, whereas the technique of introducing the gases into the chromatograph after pyrolysis is complete gives similar results to a constant-temperature sublimation technique. We also cut out the sample loop after a fixed time so that tarry materials cannot enter the column-detector circuit.

It is possible to use a metal sample holder for the polymers and induce heat in it to pyrolyse samples or, alternatively, mix a metal with the polymer and use it to pyrolyse. The latter technique was chosen because it allows a very intimate mixture of metal and polymer to be obtained and therefore homogeneous heating of the sample. Plaskon metal, commonly used for induction heating of steel samples, was used. In addition, in some runs a very fine iron powder was added to obtain very intimate mixtures. A 10/30 ground-glass sample tube was used with the metal sample mixture. The sample was held by glass wool plugs at a fixed geometry.

The chromatographs for a polyurethane polymer pyrolysis is shown in Fig. 1. The upper curve represents the technique of pyrolysing while the helium stream passes over the sample ; the lower is that where the pyrolysis is done in a vacuum and then the products are introduced in the helium stream. The point where the furnace is 'fired' gives a mark on the chromatograph, the width of it being a measure of the firing. The first peak is an air peak since some air is always trapped in the solids and released when they are heated. We note a similar pattern is obtained for both techniques, but slight peak displacement is obtained. Sufficient polymers have been run to show this displacement always occurs. For the first technique discussed above, the peaks appear at slightly longer times. It appears better separation of components is also obtained by this first technique as illustrated by the lack of tailing in the long-time peaks of the upper chromatographs.

While more work will be required to establish the best conditions for pyrolysing samples, work to date suggests the first technique has a good deal of promise. A number of variables must be tested, including length of pyrolysis, column packing and temperature, sample geometry and preparation.

A number of interesting experiments suggest themselves for this system. For example, catalytic effects could be studied by introducing catalysts into the sample. Oxidizers could also be introduced to give oxides of the pyrolysis products and these

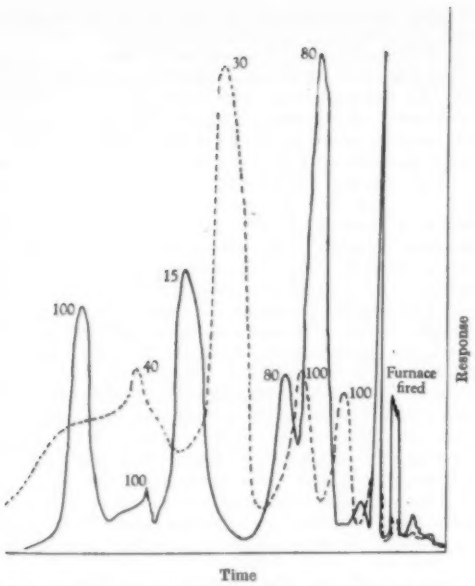

Fig. 1. Upper curve is the chromatograph of a polyurethane pyrolysate using the technique of introducing the gaseous products into the helium stream during pyrolysis. Lower curve is a similar pyrolysate which was introduced into the helium stream after pyrolysis is complete. Silicon rubber column; 130° C.; chart paper ¼ in. per min.; flow-rate 100 c.c. per min. Attenuator readings are given at each peak; 100 being equivalent to full gain setting.

could be studied. Solids, high-boiling and viscous liquids will also be attempted in later work. Kinetic studies on polymer ageing, as well as other systems could also be done.

Harms has reported how the infra-red spectra of pyrolysates can be used for identification[3]. By standardizing our technique a similar identification could be done.

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Heterogeneous Catalysis in Hydroformylation

The original observers of the hydroformylation (Oxo) reaction assumed heterogeneous catalysis. Subsequent workers have attributed, either by specific hypothesis or apparent assumption, both hydroformylation and concurrent hydrogenation (of aldehyde) to homogeneous catalysis by dicobalt octacarbonyl or cobalt hydrocarbonyl. Our recent results, which indicated a heterogeneous character of hydroformylation via cobalt catalysis[1], made it appropriate to wonder if hydrogenation under these conditions were not also in reality heterogeneously catalysed.

The evidence on which arguments for homogeneous catalysis of hydrogenation have been based consists of observations that sulphur compounds and carbon monoxide, which are known to be poisons for metallic hydrogenation catalysts, do not poison this hydrogenation[2]. It is now proposed that these previous observations can be rationalized in terms of a heterogeneous mechanism if the dynamic equilibrium between metallic cobalt and the cobalt carbonyls is taken into account. It has been pointed out that if cobalt carbonyl is subjected to hydroformylation conditions, a precipitation of cobalt occurs in the reactor, and conversely that cobalt carbonyl is formed if metallic cobalt is subjected to these conditions[3]. Also, it has been observed that in the presence of organic materials cobalt hydrocarbonyl decomposes to the metal, tetracobalt dodecarbonyl, carbon monoxide and hydrogen rather than to hydrogen and dicobalt octacarbonyl[4]. Applying this concept of the nature of the catalyst to the mechanism of hydrogenation, it becomes readily understandable that surface poisons should not be effective on a cobalt surface in such a dynamic equilibrium system, since the metal is constantly being solubilized and re-deposited. Each such creation of fresh surface allows the aldehyde to compete with the poison for this surface.

It is thus evident that in order to test adequately the heterogeneity of this hydrogenation catalysis, it is necessary to study poisons which affect metallic catalysts in a fashion more fundamental than blocking of surface adsorption. Such poisons are the heavy metals, which enter into the solid catalyst phase and poison its activity for hydrogen reactions by filling the *d*-band holes with the outer electrons of the poison[5,6]. Experiments in which ions of lead, mercury and bismuth are added in oil-soluble form to a hydroformylation reaction indeed show the anticipated poisoning effect (Table 1).

Table 1. Heavy Metals as Hydrogenation Poisons in Hydroformylation Media*

Run No.	Metal ion added	Metal ion (gm. atom/l.)†	$Cobalt^{2+}$ (gm. atom/l.)†	Olefin conversion (mole per cent)	Hydrogenation of aldehyde (per cent)
1–5	None	—	0·020	81·8	90·0
6	$Lead^{2+}$	0·0040	0·020	72·1	22·8
17	$Mercury^{2+}$	0·0040	0·020	80·5	70·8
29	$Thallium^{3+}$	0·0040	0·020	78·8	91·0
40	$Bismuth^{3+}$	0·0018	0·020	76·6	43·0

* Conditions were C_7 olefin (mixed isomers), 177° C., 6 hr. reaction time, 3,000 *g* lb./sq. in. maximum pressure, hydrogen partial pressure varied as the run proceeded from 1,750 to as low as 1,230 *g* lb./sq. in., depending on the amount of hydrogenation which occurred in the given reaction.
† All metals were added in ionic form. Undoubtedly the bulk of metals do not remain in ionic form, hence concentrations are recorded in gm. atom/l.

Conversely, thallium does not poison the hydrogenation. The oxidation-reduction potentials are such that ions of lead, mercury and bismuth should be reduced to the metallic state when brought into contact with metallic cobalt, whereas the thallic ion should be reduced only to the thallous state.

This experimental demonstration of poisoning of hydrogenation by a recognized class of poisons for metallic catalysts, together with a rationalization of the inactivity of the class of poisons previously studied[2], indicates that hydrogenation under hydroformylation conditions in reality proceeds via a heterogeneous mechanism in which metallic cobalt is the catalyst.

A full report on this work will be published elsewhere in the near future.

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BIOPHYSICS

Thermal and Electrical Properties of Nucleic Acids and Proteins

IN 1955, Duchesne and Monfils[1] discovered absorption lines in the frequency-range of 30 Mc./sec. in the sodium salts of deoxyribonucleic acid and nucleoprotein of yeast and of ribonucleic acid of *Escherichia coli*, all in the dry state, when these substances were inserted in the condenser of a super-regenerative oscillator.

It was clear from a detailed study of the whole question[2] that the main factor determining the occurrence of these lines was the piezoelectric character of the substances, and that they originated from mechanical movements of large groups of particles inside the crystals, or perhaps, in the case of large systems such as those under consideration, inside the molecules themselves. This same remarkable piezoelectric property has recently been observed and analysed by Polonsky, Douzou and Sadron[3] using deoxyribonucleic acid of different origins, and it was further discovered by these authors that these substances were ferroelectric, with a Curie point at about 50° C.

In our method[1,2], it was shown that the lines are reversibly shifted by temperature and that the displacements called Δ are given by:

$$\Delta = -\frac{1}{\nu}\frac{\mathrm{d}\nu}{\mathrm{d}T} = \alpha\,\gamma$$

where α is the thermal expansion coefficient (in volume) of the substance, and γ the Grüneisen constant. On applying this formula to the deoxy- and ribo-nucleic acids and nucleoprotein already mentioned, it was found that the Δ's reached a remarkably low value comparable to that known for quartz and metals, and in fact a hundred times less than those we had measured for ordinary organic compounds.

We have now extended our earlier investigation to include deoxyribonucleic acid of various other kinds, and also some proteins. Further, as a consequence of the low values of the Δ's, it was possible to infer, according to well-known empirical relationships[4], that thermal and, perhaps, electrical conductivities ought to be exceedingly high. With the view of verifying this inference, it was also decided to perform experiments designed to measure the latter properties.

Calf thymus and herring sperm deoxyribonucleic acid on one hand, and rabbit myosin and actomyosin, as well as collagen, on the other hand, were studied in the form of pellets which were prepared at a pressure of 700 kgm./cm.^{2}. All the compounds were characterized by a few lines especially in the region 33–35 Mc./sec., so that piezoelectricity seems to be a rather general property not only of the nucleic acids but also of the proteins. The frequency shifts which were measured over a temperature range 77–296° K., led to Δ's the approximate values of which were respectively 50, 56, 85, 100 and 47×10^{-6} unit. It was found that the absorption lines disappear around 323°K. in the case of the deoxyribonucleic acid. It is to be noted that the accuracy of the measurements was excellent for the herring sperm deoxyribonucleic acid, in which absorption lines were intense and well defined. In all other cases, it was much less satisfactory because the lines were considerably broader. The order of magnitude of the Δ's is unmodified in the deoxyribonucleic acid series, including those which were measured earlier, and among the proteins the values corresponding to myosins seem to be the highest. In this connexion, the nucleoprotein measured previously was characterized by a Δ definitely greater than in the corresponding deoxyribonucleic acid, and this may result from the influence of the combined protein.

We have also measured the electrical conductivities. As single crystals were not available, we used specimens in the powdered or fibrous state. The samples were generally in the form of a pellet of about 0·3 cm. thick and 1·3 cm. in diameter. The average value of the pressure used to prepare the pellets was 700 kgm./cm.^{2}. The specimens were then compressed between brass electrodes. The system was placed in a closed tube filled with dry air and was heated in a thermostat. The electrical resistance was measured using a commercial megohmmeter (B.P.L. *RM*-175), the applied voltage being 500 V.

In the series of biological substances examined, the variation of the d.c. electrical conductivity with temperature was found to follow the well-known equation for semi-conductors:

$$\sigma = \sigma_0 \exp(-E/2kT)\ \Omega^{-1}\ \mathrm{cm.}^{-1}$$

The activation energies found in the range 273–313° K. were: herring sperm deoxyribonucleic acid 1·80 eV., calf thymus deoxyribonucleic acid 1·80 eV., myosin 1·75 eV., collagen 0·9 eV. Despite the fact that the two samples of deoxyribonucleic acid were not only of different origins but were also in different forms (calf thymus deoxyribonucleic acid was not compressed and was used in its natural fibrous state), they were found to have practically equal E. The constant σ_0 of the herring sperm deoxyribonucleic acid, which was less reproducible than the activation energy, was of the order of magnitude of $10^3\ \Omega^{-1}$ cm.$^{-1}$. The activation energies must not be considered as very accurate not only because of lack of homogeneity of pellets but also because they are presumed to depend to a certain extent on the quantity of adsorbed water. A sample of herring sperm deoxyribonucleic acid was irradiated with a dose of 10^8 roentgens of gamma-rays of cobalt-60 and no noticeable change was measurable in its semiconductivity. As the current through the substances reaches a steady value in a few seconds, it seems that the main contribution to the conductivity should be

due to the motion of electrons. This would indeed be in agreement with recent discoveries of Blumenfeld *et al.*[5], according to which the anomalous magnetic characteristics of nucleic acids found by electron spin resonance are largely connected with the electric anisotropy of the systems.

On the other hand, it seems that the activation energy of myosin is particularly small in comparison with the other proteins, for which values as high as 3·0 eV. are fairly commonly found[6]. The values obtained for σ_0 were about 5×10^3, which is exceptionally low when compared with that for deoxyribonucleic acid. For collagen, the constant σ_0 may be estimated at $4 \times 10^{-3}\ \Omega^{-1}\ \text{cm.}^{-1}$.

We believe that all these remarkable and very intimately related properties characterizing nucleic acids and nucleoproteins, as well as proteins, must play a large part in the specific biological behaviour of these substances. Indeed, as a result of their well-known peculiar structure, the individual molecules as such may be responsible for most of the properties described here. Experiments now in progress in our laboratory have been devised to test these views.

We thank Dr. G. Hamoir for generously supplying us with samples of myosin.

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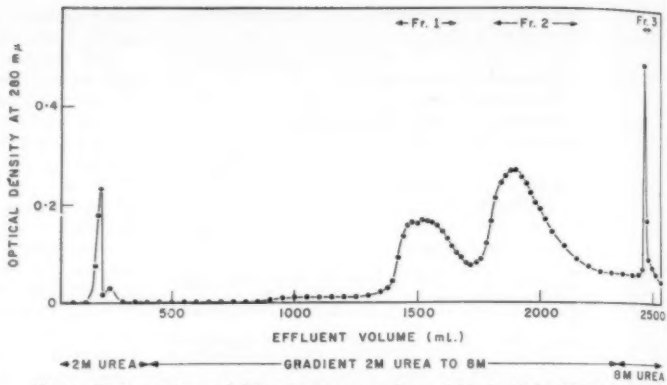

Fig. 1. Elution pattern of globin from horse oxyhæmoglobin treated with iodoacetamide. Column, 60 cm. × 2·2 cm. of 'Amberlite *CG*-50' type 2 resin. Elution with urea gradient, 2–8 *M*, *p*H 1·9

BIOCHEMISTRY

Identification of the Black Sub-Unit of the Crystallographic Model of Horse Hæmoglobin with the Valyl-Glutaminyl Polypeptide Chain

The three-dimensional Fourier synthesis of horse hæmoglobin showed four sub-units which were identical in pairs[1]. In the model of the molecule, these two kinds of sub-units were painted black and white for distinction, the chief difference being the presence of one reactive sulphydryl group in each of the two black sub-units and their absence from the white ones.

Chemical and physico-chemical methods have shown that horse globin consists of two types of polypeptide chains and each chain is equivalent to one-quarter the molecular weight of hæmoglobin[2–4]. Procedures for the separation of these two types have been devised[3,5]. One type has the N-terminal sequence valyl-leucyl (*vl*-chains) and the other valyl-glutaminyl (*vg*-chains)[6,7]. Each of the two types of chain contains one residue of cysteine[8], but only in one type is the cysteine reactive in the native protein. By determining whether the *vl*- or the *vg*-chain carries the reactive cysteine, we have now been able to correlate the chemical sub-units with those found by X-ray analysis.

Treatment of native hæmoglobin with iodoacetamide should affect cysteine residues on the black sub-units only and give rise, after acid hydrolysis, to S-carboxymethyl cysteine. Riggs and Wells[9], by a similar method involving N-ethyl maleimide, have located the more reactive sulphydryls of human hæmoglobin on the β- or valyl-histidyl-chains.

The red cells of fresh oxalated horse blood were washed several times with saline and lysed by dilution with water. After removal of cell debris by centrifugation, a ten-fold excess of iodoacetamide was added. After 1 hr. at room temperature, excess reagent was removed by dialysis against 0·01 *M* ammonium phosphate, *p*H 7. The oxyhæmoglobin was crystallized by the addition of ammonium sulphate to 2·0 *M*. The crystals were filtered off, washed with ammonium sulphate solution, packed wet in a plastic vial and sent across the Atlantic by air mail. On arrival they were put in a refrigerator, but transformation to methæmoglobin had occurred.

The methæmoglobin was reduced in 0·01 *M* phosphate buffer *p*H 7 with a five-fold excess of ammonium ferrotartrate and dialysed against water. Globin was precipitated with acid-acetone[3] and fractionated by the chromatographic procedure of Wilson and Smith[5]. The preliminary slurrying of globin solution with a portion of resin before addition to the column was omitted. Fig. 1 shows the elution pattern and the fractions selected.

Amino-acid analyses of samples hydrolysed in 5·7 *N* hydrochloric acid in sealed tubes for 24 hr. at 105° C. were made, using a Beckman-Spinco amino-acid analyser and the procedures of Spackman, Moore and Stein[10]. The averages of duplicate analyses (uncorrected for decomposition or incomplete hydrolysis) are listed in Table 1 as μmoles of amino-acid relative to aspartic acid = 14·0.

Table 1. Recoveries of Amino-Acids from 24-hr. Hydrolysates of Globin Fractions

Amino-acid	Fraction 1 (μmoles)	Fraction 2 (μmoles)	Fraction 3 (μmoles)
Lysine	11·3	10·8	—
Histidine	10·4	8·8	—
Arginine	3·1	3·9	—
Cysteic acid	0·5	0·1	0·1
S-carboxymethyl cysteine	0	0·6	0·4
Aspartic acid	14·0	14·0	14·0
Threonine	8·7	3·4	4·5
Serine	11·2	5·4	7·0
Glutamic acid	4·8	12·7	12·2
Proline	6·2	5·1	5·5
Glycine	10·6	13·0	12·9
Alanine	16·5	13·8	14·3
Valine	12·8	14·1	14·9
Methionine	1·0	0·9	1·0
*Iso*leucine	0	0	0·3
Leucine	22·3	19·2	19·5
Tyrosine	2·8	2·9	2·6
Phenylalanine	7·1	7·7	7·7

Except for the presence of cysteic acid, fraction 1 has the composition of 24-hr. hydrolysates of the *d*-chain, and excepting S-carboxymethyl cysteine and cysteic acid, fraction 2 that of the *vg*-chain. The small amount of *iso*leucine in fraction 3 is likely to be due to some contaminating protein; otherwise its composition is similar to that of the *vg*-chain.

S-carboxymethyl cysteine was present in fractions 2 and 3 only; none could be detected in the hydrolysate of fraction 1. The valyl-glutaminyl chains must then correspond to the black sub-units of the crystallographic model.

The yield of S-carboxymethyl cysteine, about 0·6 mole/mole polypeptide, is similar to that found earlier[5]. The nature of the oxidation that converted oxyhæmoglobin to methæmoglobin and unreacted cysteine to cysteic acid is being investigated. The occurrence of this oxidation, however, does not invalidate the identification of the black sub-unit with the valyl-glutaminyl polypeptide.

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Production of Acid Mucopolysaccharides by Fibroblasts in Cell Cultures

Acid mucopolysaccharides characteristic of connective tissue ground-substance are produced in tissue culture by fibroblasts from a variety of tissues of mesenchymal derivation[1–4]. It would appear that in the conditions of growth in tissue culture the spectrum of acid mucopolysaccharides typical of a given tissue[5] is not reproduced. Rather the results suggest that the cultured cells, whatever their tissue of origin, revert to a similar pattern with respect to production of acid mucopolysaccharides in that all secrete into the medium a major fraction of hyaluronic acid and a smaller component of sulphomucopolysaccharide, presumably chondroitin sulphate *C* [2,3]. Moreover, the present experiments show that production of acid mucopolysaccharides by 'stock' strains of fibroblasts may continue in tissue culture for long periods of time, up to years.

In order to assess the effects on synthesis of acid mucopolysaccharides of different conditions of growth and nutrition, it was first necessary to devise reliable methods of measuring accurately the amounts of acid mucopolysaccharides produced per cell during any given interval. Only in this way would it be possible to gain information about such issues as the relationship between the rate of cellular proliferation, cell concentration and composition of medium to the formation of a specific product, the acid mucopolysaccharides.

To this end, series of replicate cell cultures were prepared. Cell suspensions derived from trypsinization of the primary outgrowth of osteogenic fibroblasts from explants of stripped new-born rat calvarium were rendered uniform and dispensed in identical aliquots into *T*·15 culture flasks, each of which then contained approximately the same initial number of cells. Cultures were washed and fed with fresh medium usually every 72 hr. (except as otherwise indicated), each interval constituting a feeding period. 'Used' media withdrawn at each feeding were saved for analysis. The cells grew well on the glass floors and preserved a uniform appearance. They were collected at intervals from groups of flasks for determination by deoxyribonucleic acid (by the diphenylamine method as adapted by Zamenhof[6] and modified by Burton[7]), and acid mucopolysaccharides (by carbazole determination of uronic acid content from fractions obtained either after exhaustive hyaluronidase digestion, or a protamine precipitation method modified from Bollet[8]). Results were expressed as a ratio of the amount of acid mucopolysaccharides or acid mucopolysaccharides-uronic acid per μgm. of deoxyribonucleic acid per flask, the specific production, and as a rate, the specific production per hour. The mean amount of deoxyribonucleic acid present over a given period was calculated whenever possible as a more representative value than either the initial or terminal deoxyribonucleic acid values for that period.

Production of acid mucopolysaccharides on growth media. At moderate rates of growth in a 'biological' medium consisting of 20 per cent human cord serum, 50 per cent beef amniotic fluid, and 30 per cent Earle's balanced saline solution, the acid mucopolysaccharides uronic acid : deoxyribonucleic acid ratio ranged from 1·6 to 4·0 (mean = $2·75 \pm 0·18$). This average corresponds to approximately 47×10^{-12} gm. acid mucopolysaccharides per average cell, if it is assumed that each cell is equivalent to a diploid rat cell containing $6·8 \times 10^{-12}$ gm. of deoxyribonucleic acid (Leslie, 1955), and that its uronic acid content constitutes 40 per cent of the acid mucopolysaccharide molecule.

Analysis of specific production and its rate by intervals revealed that within 20 hr. after the first feeding following set-up (that is, Period II of Table 1) a specific production of 1·83 μgm. acid mucopoly-

Table 1. Rates of Growth and Production of Acid Mucopolysaccharides by Cultures of Fresh Rat Cells in the Interval between Successive Changes of Medium
(Exp. No. 50—Medium No. 5)

Period	Hours from last feed	Net supernate AMPS–uronic acid μgm./flask	DNA μgm./flask	Cell-bound AMPS–UA	Specific AMPS–UA production (μgm./μgm. mean DNA)	Rate constant spec. prod./hr.
I	50*	3·98	1·13	—	—	
II	20	3·07	—	—		
	79	2·32	1·81	0·7	1·83	0·092
		5·72	2·62	0·4	3·10	0·023
		(± 0·63)	2·50	0·55		
III	12	1·61	2·26	0·8	0·79	0·066
	34	2·00	2·30	0·8		
		5·37	3·12	0·6	2·07	0·062
	50	5·42	2·90	0·65		
		6·72	2·93	0·65	2·46	0·029
		6·92	3·05	0·55		

* Refers to hours after initial set-up.
AMPS, acid mucopolysaccharides; UA, uronic acid; DNA, deoxyribonucleic acid.

saccharides–uronic acid/μgm. mean deoxyribonucleic acid had occurred, while the deoxyribonucleic acid had increased 60 per cent, its maximal rate of increment. The amount of acid mucopolysaccharides released in this time was 47 per cent of the total produced over the whole (79 hr.) feeding period. In the next 59 hr. of this period, deoxyribonucleic acid increased an additional 41 per cent, during which time specific production was 1·4 μgm. acid mucopolysaccharides–uronic acid/μgm. mean deoxyribonucleic acid and the production-rate was 0·023, a decrease of 75 per cent. The acid mucopolysaccharides–uronic acid/final deoxyribonucleic acid ratio for the whole 79-hr. feeding period was 2·24; specific production for the whole period on the basis of the mean deoxyribonucleic value was 3·1. Within period III, that is, the subsequent period following the second feeding, the same relationships obtained, so that in the segment of this period during which the rate of increase of deoxyribonucleic acid was greatest, that is, the first 34 hr., production-rate was also greatest. Such results suggested a direct, rather than a reciprocal, overall relation between rate of cell population increase and synthesis of acid mucopolysaccharides in a relatively rich medium promoting moderate growth. With still higher rates of growth (obtained on a low-serum growth-stimulating medium consisting of 5 per cent. cord serum, 75 per cent Eagle's medium and 20 per cent whole egg ultrafiltrate) the increment of acid mucopolysaccharides produced did not keep pace with the increase in deoxyribonucleic acid; specific production was generally not as high as that measured during comparable periods of moderate growth on high serum media with amniotic fluid instead of whole egg ultrafiltrate.

Conversely, when cultures nourished on these growth media became 'crowded', that is, as the cells of the monolayer became contiguous, the rate of cell proliferation declined. This reduced growth was accompanied by a decreased specific production of acid mucopolysaccharides.

Production of acid mucopolysaccharides on maintenance media. Maintenance media consisting of 2 per cent dialysed cord serum, Earle's balanced saline and variable proportions of Eagle's medium supported seemingly healthy cell life, but with little or no growth, for six or more feeding intervals. Increased proliferation could be effected in such media by augmenting the proportion of Eagle's medium. Acid mucopolysaccharides continued to be produced by cells in maintenance media, in some instances attaining a specific production ratio as high as 1·0; but in no case was specific production greater than 1·0; more usually it was less (Fig. 1). Addition of glucose, known to be a substrate for synthesis of acid mucopolysaccharides, in concentrations of 0·04–0·3 per cent in maintenance medium has no appreciable effect on specific production.

Distribution and kind of acid mucopolysaccharides produced in cell culture. A fraction of the total amount of acid mucopolysaccharides synthesized in any culture remained bound to the cells after washing with either warm or cold saline. This cell-bound acid mucopolysaccharide usually amounted to about 10 per cent of that secreted into the medium. However, in conditions of crowding, the proportion of cell-bound acid mucopolysaccharides to the total increased markedly and reached high levels in extremely dense 'stock' cultures. In some series of analyses of very crowded non-growing stock cultures, specific production tended to be stabilized at about 0·6.

The acid mucopolysaccharides produced by both stock strains of rat osteogenic fibroblasts and recently isolated cell lines was predominantly non-sulphated, and had the properties of hyaluronic acid. After addition of sulphate labelled with sulphur-35 to the

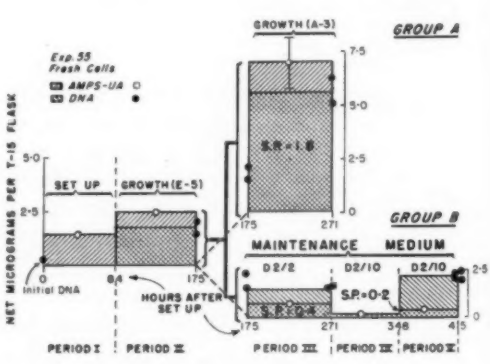

Fig. 1. Growth and production of soluble acid mucopolysaccharides over successive feeding periods by cell cultures of recently isolated rat fibroblasts. Cultures were grouped at random and transferred to either growth or maintenance medium at the end of period II. Differences in growth and total and specific production of acid mucopolysaccharides (see text) 96 hr. later are graphed. Slight growth and production of acid mucopolysaccharides continued on maintenance medium
AMPS, acid mucopolysaccharides; UA, uronic acid; DNA, deoxyribonucleic acid

medium, sulphate was fixed in not more than 5–10 per cent of the acid mucopolysaccharides secreted by the fibroblasts. Chemical fractionation and analyses of the acid mucopolysaccharides produced by cultured fibroblasts are in progress.

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A Rapid Dialyser for Small Samples

While purifying enzymes, it became necessary to dialyse small amounts of a suspension with maximum efficiency, without allowing the precipitate to settle. This led to the design of a rapid dialyser of simple construction, which we call a 'flat dialyser'.

The dialysis cell consists of a frame (Fig. 1) cut from a 1-mm. thick 'Plexiglas' sheet. This is slipped into previously moistened Visking seamless cellulose tubing ($2\frac{3}{8}$ in. wide: for sizes of tubing mentioned later only the inflated diameter will be given), inside which it fits snugly, leaving about 5 cm. of tubing on each side. One of the ends of the tubing is then wound on a 'Plexiglas' strip (0·3 × 0·7 × 7 cm.) and fastened on to the frame with a wide rubber band *F* (Fig. 2). If the length of the tubing has been correctly chosen, in the last turn some tension will be applied to the membrane, thus stretching it over the frame. The solution to be dialysed (up to 1·5 ml.) is then introduced from the open end with a Pasteur pipette, and most of the excess air is driven out by pressing the cellulose tubing between the fingers. The open side of the cell is then closed in the same way as the other

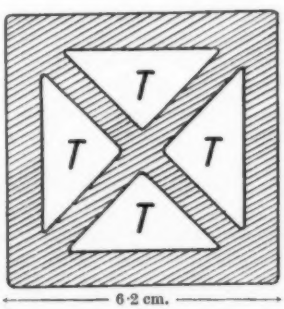

Fig. 1

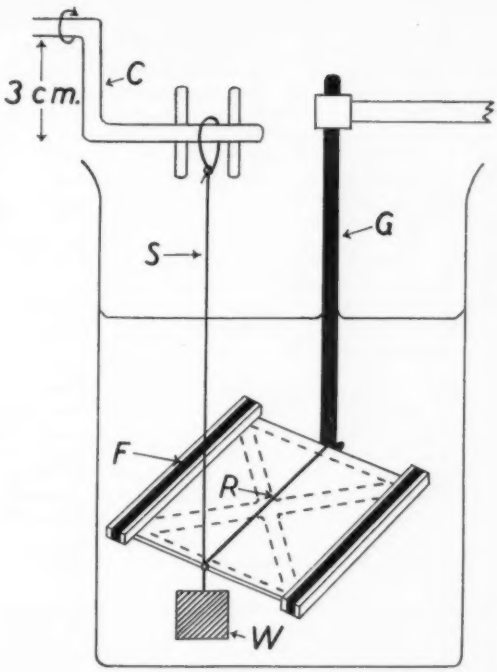

Fig. 2

one. The assembled dialysis cell is inserted into a rubber band *R*, which is tied on one side to a glass rod *G*, supported by a clamp, and on the other side to a weight *W* and to a length of string *S*. The other end of *S* is made into a loop and hooked from the glass crank *C*, which is driven by a motor at about 60 r.p.m., thus imparting an up-and-down motion to the dialysis cell. The air bubbles entrapped, together with the liquid in the triangular spaces *T*, help to stir the solution. The whole apparatus is placed in a 1,000-ml. beaker, containing at least 600 ml. of liquid. When the dialysis is completed, one side of the cell is unrolled, the cell is held in an oblique position and the liquid is sucked out with a Pasteur pipette.

This arrangement was compared with other methods by dialysing 1 ml. samples of 0·1 *M* sucrose at 1° C. against 800 ml. of water for different times, and analysing the solution that remained in the bag. The results, corrected for changes of volume during dialysis, are shown in Fig. 3. Most of the points are average values of duplicate, and in somes cases triplicate, experiments. Under condition *A*, 8/32 in. cellulose tubing containing the sample was tied on both ends, leaving a small bubble of air inside and placed in a beaker provided with a magnetic stirrer. Condition *B* was similar but the diameter of the tubing was larger (18/32 in.) and about three-fourths of the inner space were occupied by air under a slight pressure. When the magnetic stirrer was set at a high speed, the bag revolved on its vertical axis so rapidly that the liquid rose on to the sides, thus increasing the useful surface for diffusion and probably the internal agitation. In order to eliminate possible discrepancies arising from variations in permeability of the different sizes of cellulose tubing used[1], condition *A* was repeated with the 18/32 in. tubing. This arrangement is called condition *C*. Condition *D* refers to an 8/32 in.

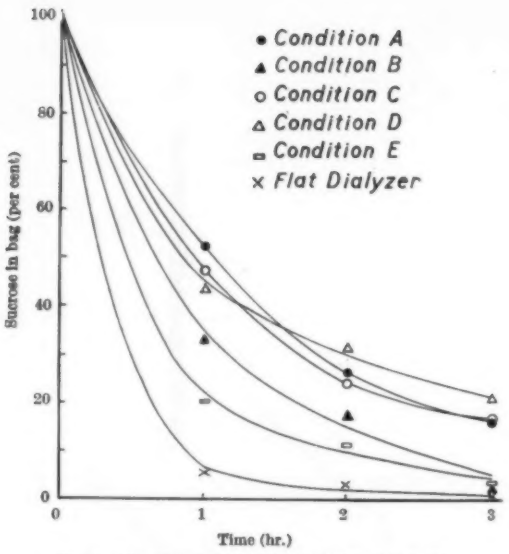

Fig. 3. Time-course of dialysis with different methods

tubing, containing an air bubble and a glass bead and placed in a rocking dialyser. Finally, condition *E* was the arrangement first proposed by Seegers[1,2], where a glass tube closed at both ends was placed in the cellulose bag, thus confining the solution to be dialysed to a thin layer in the annular space formed. In this case also the bag was placed in a rocking dialyser.

It can be seen in Fig. 3 that conditions *A*, *C* and *D*, with a membrane surface about a quarter that of the flat dialyser, gave similar results, while condition *B* was appreciably superior. The flat dialyser was the most efficient, followed by condition *E*. Since in the last two cases the membrane surface in contact with the inner liquid was about the same, the difference was probably due to the internal stirring obtained in the flat dialyser. It should be noted that condition *E* was unsuitable for our particular purpose, because the precipitate sedimented during the run.

In another experiment 2 *M* ammonium sulphate was used. After 30 and 60 min. dialysis under condition *A* the amount of salt remaining in the bag was 40 and 13 per cent respectively. The corresponding values for the flat dialyser were 3·8 and 0·6 per cent.

We are indebted to our colleagues of the Instituto de Investigaciones Bioquímicas 'Fundación Campomar' for many useful discussions. This work was supported in part by a research grant (No. *G*-3442) from the National Institutes of Health, U.S. Public Health Service and by the Rockefeller Foundation.

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Phenazine Methosulphate as a Mediator in the Oxidation of Pyruvate by Pyruvate Decarboxylase from Brewer's Yeast

Purified pyruvate decarboxylase from brewer's yeast[1] is not only capable of decarboxylating pyruvate to acetaldehyde and carbon dioxide[2], but can also catalyse the oxidation of pyruvate to acetate with 2,6-dichlorophenolindophenol as artificial hydrogen acceptor[3]. Ferricyanide cannot act as a hydrogen acceptor with pyruvate decarboxylase irrespective of whether the enzyme is prepared from yeast[3] or wheat germ[4].

We now find phenazine methosulphate to be an excellent electron carrier for the oxidation of pyruvate by pyruvate decarboxylase from brewer's yeast. Although phenazine methosulphate is not reduced to any measurable extent as no extinction changes were observed at 366 and 405 mμ, it accelerated the reduction of 2,6-dichlorophenolindophenol by some 120 per cent and made possible the otherwise scarcely measurable reduction of ferricyanide (Fig. 1).

The reaction-rate is not dependent on the concentration of ferricyanide. At *p*H 7·4 there is significant non-enzymatic reduction of 2,6-dichlorophenolindophenol and ferricyanide respectively, but under the conditions of our experiments (*p*H 6·0) the non-enzymatic reaction is negligible. That phenazine methosulphate works only as a carrier, and is not itself reduced to a measurable extent could be related to its negative redox potential[5].

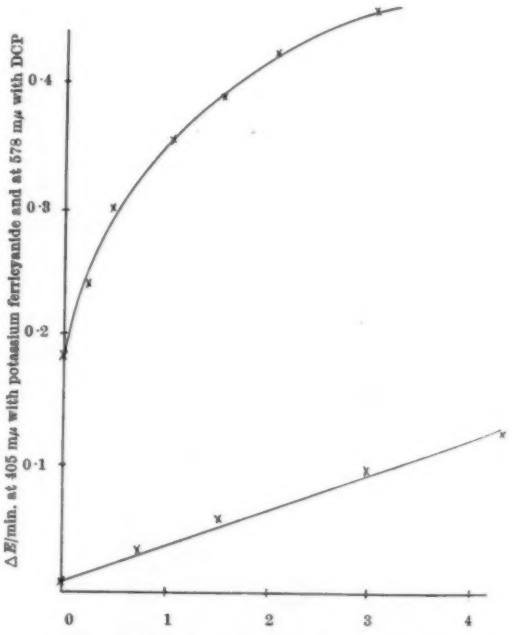
ΔE/min. at 405 mμ with potassium ferricyanide and at 578 mμ with DCP
Phenazine methosulphate concentration in gm./ml. × 10³ with DCP and gm./ml. × 2·10⁵ with potassium ferricyanide

Fig. 1. Acceleration of reduction of DCP and potassium ferricyanide by addition of varying concentrations of phenazine methosulphate. In cuvette (d = 1 cm.) 1·0 ml. *M*/20 pyruvate, 1·8 ml. *M*/6 citrate/sodium hydroxide buffer *p*H 6·0, 0·01 ml. purified yeast carboxylase[1] (protein content as above), and DCP or potassium ferricyanide as detailed above; total volume 3·0 ml. Upper curve, 40 μgm. DCP/ml.; 30 μgm. enzyme protein/ml.; lower curve, *M*/300 potassium ferricyanide; 300 μgm. protein/ml. DCP = 2,6-dichlorophenolindophenol

In recent experiments with pyruvate labelled with carbon-14, compounds of pyruvate and acetaldehyde with thiamine pyrophosphate (activated pyruvate and activated acetaldehyde) were found to be intermediates of pyruvate decarboxylation[6]. Considering these findings and other previous experiments on the oxidation of pyruvate with 2,6-dichlorophenolindophenol[3] a possible reaction sequence which would account for the effects illustrated in Fig. 1 would be: pyruvate → α-lactyl-thiamine pyrophosphate (activated pyruvate) → α-hydroxy-ethyl-thiamine pyrophosphate (activated acetaldehyde) → α-oxoethyl-thiamine pyrophosphate (acetyl-thiamine pyrophosphate) → acetate, the penultimate step being brought about by phenazine methosulphate and 2,6-dichlorophenolindophenol or ferricyanide.

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Elution of Alkaloids from Citrate-buffered Paper Chromatograms

ONE of the most satisfactory methods of paper chromatography of alkaloids is the butanol–citrate system introduced by Curry and Powell[1]. It suffers, however, from the disadvantage that if one attempts to elute the alkaloid with chloroform for subsequent confirmatory tests, a certain amount of citrate is also extracted. This interferes with certain important colour tests, as the yellow colour which it gives with concentrated sulphuric acid modifies any colour given by the alkaloid. For example, morphine with the Marquis reagent gives a muddy brown instead of a clear violet.

This drawback can be overcome by converting the citrate to the barium salt, which is much less soluble in organic solvents. The chromatogram spot is cut out and, if the paper has been sprayed with iodoplatinate or iodobismuthate, decolorized with a drop of 10 per cent sodium sulphite solution. It is then dried, treated with a drop of a 10 per cent solution of barium chloride, re-dried and the free base liberated by the addition of a drop of concentrated ammonium hydroxide solution. After again drying, the alkaloid is eluted with chloroform[2,3], and its identity confirmed by suitable colour and micro-crystal tests[4].

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Production of D-Araboascorbic Acid by *Penicillium*

WE have found that some species of *Penicillium* produce D-araboascorbic acid. Rarely has this acid been found in biological material or products. Isherwood *et al.*[1,2] have found it in cress seedlings in D-altrono-γ-lactone solution and in the urine of a rat injected with D-mannono-γ-lactone.

P. decumbens, *P. chrysogenum*, *P. chrysogenum* mut. *fulvescens* Takashima Arima and Abe, *P. notatum*, *P. meleagrinum* and *P. cyaneofulvum* produced D-araboascorbic acid from sucrose.

The following medium was used (per cent): glucose or sucrose, 2; sodium nitrate, 0·1; ammonium sulphate, 0·1; urea, 0·1; potassium dihydrogen phosphate, 0·25; crystalline magnesium sulphate, 0·1; crystalline manganese sulphate (trace); and crystalline zinc sulphate (trace); *p*H 5·2. The *Penicillium* was incubated for five or seven days at 25–27° C. The broth showed strong reducing activity to 2,6-dichlorophenol indophenol. The contents in the broth were up to 3 mgm. per ml. After the broth was cleared of impurities, the supernatant was run through the anion resin '*IR*-4*B*' column[3]. 1 *N* hydrochloric acid solution was used in elution. The effluent was evaporated *in vacuo* to a syrup at 25–30° C. under an atmosphere of carbon dioxide. After the syrup was dried in a vacuum desiccator for three or five days, white crystals were obtained. These were recrystallized from methanol dioxane mixture. The 2,4-dinitrophenyl hydrazone was prepared from the resin effluent[4]. The chemical properties of the free crystal and the osazone are shown in Table 1 and their infra-red absorption spectra in Figs. 1 and 2.

D-Araboascorbic acid was produced from D-glucose, D-gluconate and sucrose only; but not from other carbon sources, for example, glycerin, 2-keto-gluconate, glucuronate and galacturonate. These observations make it seem possible that the conversion of carbon source into D-araboascorbic acid occurs without rupture and inversion of the carbon chain. The stereochemical relation between glucose and D-araboascorbic acid was studied by means of isotopes. The replacement culture by the intact cells

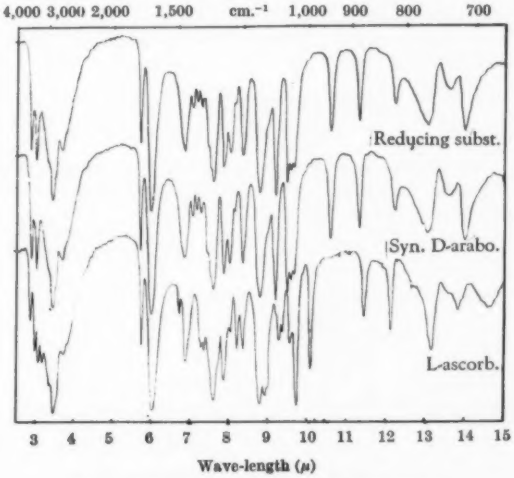

Fig. 1. Infra-red absorption spectra of free crystal

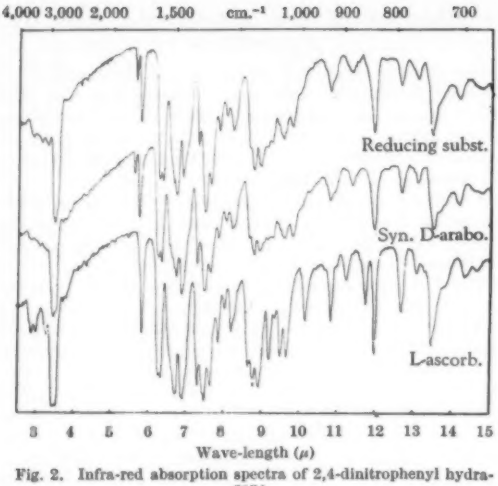

Fig. 2. Infra-red absorption spectra of 2,4-dinitrophenyl hydrazone

of *P. notatum* was carried out with D-glucose-1-^{14}C as a tracer. The D-araboascorbic acid was isolated by paper chromatography from the broth and crystallized. In order to determine the distribution of the isotopic carbon, the crystals were decarboxylated in 8 *N* sulphuric acid at 100° C. for 3 hr., and the residual, furfural, was burned and the radioactivities measured in barium carbonate[3]. It was found that D-glucose-1-^{14}C was converted to D-araboascorbic acid with 80 per cent of its activity in the carbon 1.

Table 1. Chemical Properties of the Reducing Substance

(1) Free crystal
m.p. 172° C. (uncorr.)
Anal. Calcd. for $C_6H_8O_6$ C 40·92% H 4·58%
Found C 41·27% H 4·66%
$[\alpha]_D^{26·5}$ −23° (1% in water)
Maximum absorption in ultra-violet spectrum 245 mμ (in 2 per cent hydrogen phosphate)
265 mμ (in water)

(2) 2,4-dinitrophenyl hydrazone
m.p. 238–242° C. (uncorr.)
Anal. Calcd. for $C_{12}H_{14}O_{12}N_8$ C 40·44% H 2·64% N 20·97%
Found C 41·55% H 2·84% N 21·15%

Investigations of the intermediates between glucose and D-araboascorbic acid have been carried out which indicate the following possible scheme:

D-Glucose → D-gluconate → 3-keto-D-gluconate → D-araboascorbic acid
↘ ↗
D-glucono-γ-lactone

We wish to express our thanks to Prof. T. Asai and Prof. K. Yamada, University of Tokyo, and Dr. H. Okazaki, Sankyo Co., Ltd., for their kind advice.

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RADIOBIOLOGY

Prevention of the Lethal Effect of the Decay of Incorporated Phosphorus-32 by Growth at 45°

In recent years there has been a growing conviction that understanding the effects of radiation on bacterial cells requires distinguishing between the primary radiation targets on one hand and the metabolic events which ensue, on the other[1]. Even if the primary target is, or includes, deoxyribonucleic acid, as is the case for irradiation with ultra-violet light of wave-length 2537 Å. and for X-irradiation, the probability of survival can be increased by such post-irradiation treatments as exposure to visible light[2], incubation at elevated temperature[3], antibiotic-induced inhibition of protein synthesis[4], etc.

Inactivation of bacteria by the decay of incorporated phosphorus-32 represents another instance where the targets include deoxyribonucleic acid[5]. It is therefore of interest to report that here too the lethal chain of events may be modified after primary damage has presumably occurred. Cells of *Escherichia coli* strain *B* containing phosphorus-32 which fail to form colonies if incubated at the usual temperature of 37°, will do so if incubated at 45° instead.

Carrier-free phosphorus-32 in the form of orthophosphate was obtained from E. R. Squibb and Sons, New Brunswick, New Jersey. The techniques employed to incorporate the isotope and to measure survival have been described by Fuerst and Stent[5]. The only deviation from their procedure was to freeze and store the radioactive and control aliquots at − 78° instead of − 196°. After thawing, cells were spread on the surface of two sets of nutrient broth agar plates. One set was incubated at 37° and the other at 45°. The numbers of colonies appearing were counted after 24 hr.

Non-radioactive control cells tested immediately after growth and after various periods of storage in the cold did not show a difference in colony count between plates incubated at 45° and at 37°. Cells containing phosphorus-32 also showed no difference when plated immediately after the incorporation of the isotope. The effect of 45° incubation on *B* cells tested during the course of decay is illustrated in Fig. 1. A long plateau in the curve for 45° incubation was observed in repeated experiments and a short plateau was observed occasionally in the curve for 37° incubation.

It has been shown that the cellular processes which determine the lethal and genetic effects of ionizing and ultra-violet radiation are completed in a time corresponding to less than one division[6]. By means of temperature-switch experiments[6], it was found that this generalization also applies to the lethal effect of decay of phosphorus-32. As shown in Fig. 2, when thawed and plated cells are incubated first at 37°, recovery decreases rapidly if transfer to 45° is made at later than ½ hr. Conversely, if the first incubation is at 45°, recovery begins immediately and 50 per cent of potentially reactivable cells can be rescued by 1 hr.

Fuerst and Stent[5] found that radioactive cells of *E. coli* strain 15*T*⁻, a thymine-less mutant, exhibited an increased lag before division at 37°. Control cells started to divide almost immediately, but cells containing phosphorus-32 did not begin until 1½–2 hr.

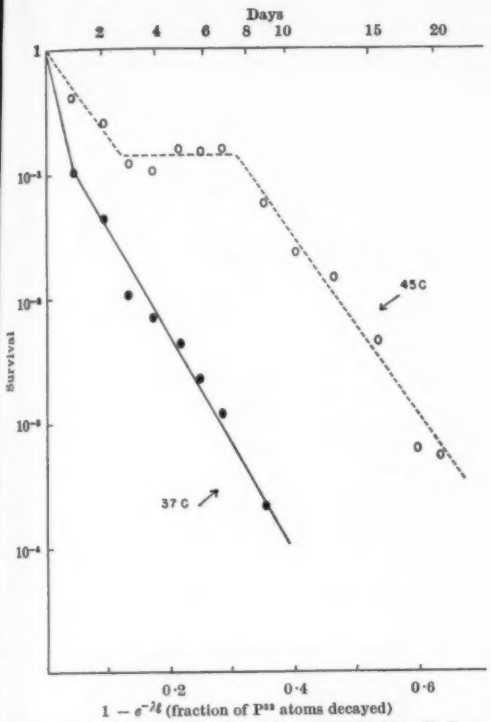

Fig. 1. Survival of phosphorus-32-containing *E. coli B* as measured by incubation at 37° and at 45°. Specific activity, 10 mc. phosphorus-32 per mgm. total phosphorus

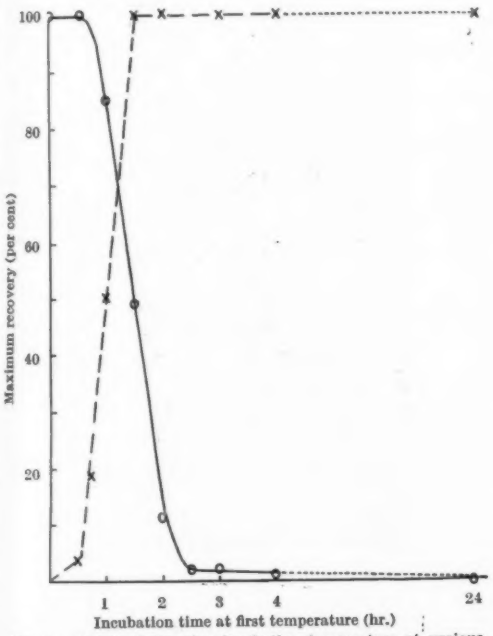

Fig. 2. Effect of changing incubation temperature at various times after plating. ○, First temperature = 37°; ×, first temperature = 45°. The data were obtained when 17 per cent of the phosphorus-32 atoms had decayed. At this time, no recovery corresponded to 0·5 per cent survival and maximum recovery to 12 per cent survival

(depending on the amount of phosphorus-32 decay that had occurred). By re-spreading experiments[7], a lag of ½-hr. was found for control *B* cells at 45° and 1 hr. for radioactive *B* cells at 45° (1 per cent survival at 37°). A point of interest is that the growth of the cells containing phosphorus-32 at 45° was synchronized, in agreement with previous observations at 37°[8].

Reduction of the lethal effect of phosphorus-32 incorporated into strain *B* could not be obtained by other treatments which are effective after irradiation with ultra-violet. Photo-reactivation was attempted by diluting thawed cells into physiological saline and exposing to light of wave-length 3650 Å. (ref. 8) for 1 hr. before plating. No increase in survival was obtained. Substitution of *M*9–agar[9] for nutrient broth agar also had no effect, that is, the colony counts on the two media were identical after 37° incubation and also after 45° incubation.

The effects of phosphorus-32 decay on the bacterial cell resemble the effects of X-rays and ultra-violet radiation in the following particulars: prolongation of the lag[10], 'reactivability' and the existence of a sensitive period during which 'reactivation' can be obtained. Although the initial physical events are quite different for these three agents, it would appear that the biological events which they trigger must have some features in common.

I wish to thank Miss Eva Simson for technical assistance.

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Effects of X-irradiation on Papillary Muscle of the Cat

A NUMBER of investigations have been carried out on the influence of X-rays on the electrophysiological and mechanical properties of striated muscle[1–5]. Most of these experiments have been performed on frog's sartorius muscle, and have revealed the fact that striated muscle generally shows a high X-ray insensitivity. Only minor changes of the membrane resting potential could be recorded during the first few hours following a heavy X-irradiation (80–250 kr.). Similar results were obtained by us (Schliep, H. J., Kraupp, O. and Pillat, B., unpublished results). A 1-mV. decrease of resting potential was produced by an average of 160 kr. (50 kV. 25 m.amp.). Further investigations on the same preparation showed that doses between 300 and 500 kr. practically did not influence intracellular action potentials recorded at

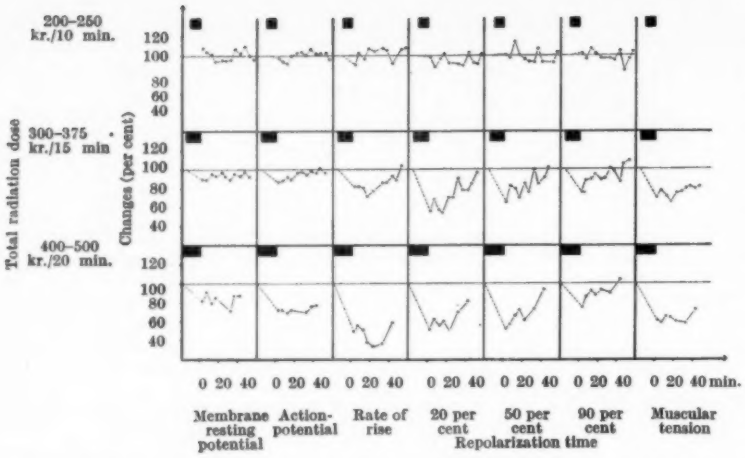

Fig. 1. Ordinate: Average percentage changes of membrane resting potential, action potential, rate of rise, 20, 50, and 90 per cent repolarization time and mechanical tension compared with the average control values of all experiments performed (100 per cent). Abscissa, Time in min. post-irradiation. Upper row, 200–250 kr./10 min; middle row, 300–375 kr./15 min.; lower row, 400–500 kr./20 min. Black bars indicate exposure to irradiation

5-min. intervals before, during and after irradiation (Kraupp, O. and Pillat, B., unpublished results).

However, no electrophysiological work concerning the effect of X-irradiation on heart muscle fibres has so far been reported. For that purpose membrane resting and action potentials were recorded with the intracellular micro-electrode technique from papillary muscles of cats. The method has been described in detail elsewhere[6]. An unfiltered X-ray source (50 kV., 25 m.amp.) was used at dose-rates between 20 and 25 kr./min. at an approximate distance of 10 cm. from the preparation.

In this way, three groups of experiments were carried out. Keeping the dose-rate constant (20–25 kr./min.), the duration of X-irradiation was varied. In four experiments the exposure to X-rays lasted 10 min., in six 15 min. and in two further experiments, 20 min.

In all these experiments measurements of membrane resting potential, action potential, rate of rise of the action potential, 20, 50 and 90 per cent repolarization time and of the mechanical tension were performed at 5-min. intervals for at least 1 hr. before and after X-irradiation.

To give a clear demonstration of our results the experiments of each group irradiated were combined. Changes of each parameter were expressed as percentages of the mean control values. As can be seen from Fig. 1, X-ray doses between 200 and 250 kr. had no significant influence on any of the parameters recorded. If the total X-ray dose was increased to 300–375 kr. definite changes of all parameters could be seen. These changes consisted in a decrease of the membrane resting and action potential, in a reduced rate of rise, and in a shortening of the 20, 50 and 90 per cent repolarization time. At the same time the muscular tension was diminished. At total radiation doses between 400 and 500 kr., the changes of all recorded parameters were even more pronounced. Two facts of interest were observed at total X-ray doses above 300 kr.: (1) The observed effects were most pronounced immediately after X-irradiation. (2) All irradiation-induced effects were reversible, at least to some extent, within 1 hr. Almost complete restitution of the normal repolarization time was found (Pillat, B., Kraupp, O., and Heistracher, P., unpublished results).

All the changes described are illustrated by a sequence of action potentials recorded before and following X-irradiation in a typical experiment (Fig. 2).

The above-described radiation-effects on heart muscle fibres resemble to some extent those obtained with 2,4-dinitrophenol or iodoacetate after incubation of rat's atrium in a solution of these substances[7]. Similarities between the effects of X-irradiation and of 2,4-dinitrophenol on striated muscle fibres have been reported by Woodbury[8]. This points to the possibility that reversible inhibition of some essential metabolic steps might be involved in the mechanism underlying the

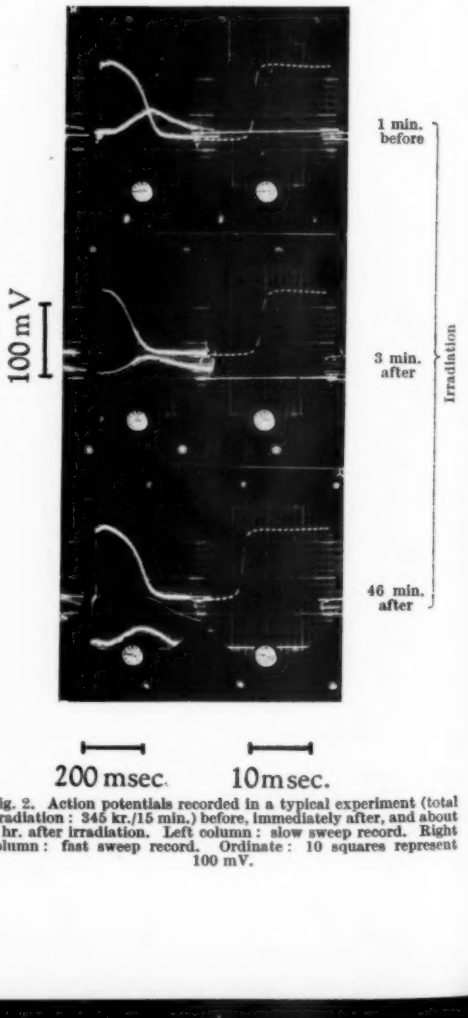

Fig. 2. Action potentials recorded in a typical experiment (total irradiation: 345 kr./15 min.) before, immediately after, and about 1 hr. after irradiation. Left column: slow sweep record. Right column: fast sweep record. Ordinate: 10 squares represent 100 mV.

observed radiation effects as reported in this communication. The question arises whether the changes are due to a direct influence of radiation on the cell membrane or to a radiation-produced chemical substance; such a primary radiochemical step could be the formation of hydrogen peroxide.

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Sensitization of *Escherichia coli* to Gamma-Radiation by N-Ethylmaleimide

With the exception of oxygen and nitric oxide, chemical agents which enhance the effect of radiation on bacteria have received little attention. In the experiments to be described, N-ethylmaleimide is shown to be a sensitizing agent for *Escherichia coli* strain *B/r*. A sensitizing agent is taken here to be one which enhances radiation-damage when added before or during irradiation but not after irradiation.

N-ethylmaleimide was obtained from the Aldrich Chemical Co.; it was dissolved in sterile 0·067 *M* phosphate buffer to make a 0·01 *M* stock solution which was kept at 3° C. diluted as required. Sterilization of this solution was not found to be necessary. 20–24 hr. cultures on nutrient agar slopes were washed off with 10 ml. of 0·067 *M* phosphate buffer (*p*H 7) and 1 ml. was diluted into a further 10 ml. buffer before use. N-ethylmaleimide was added 4–6 min. before irradiation except where otherwise stated. The suspensions were irradiated at room temperature under aerated or anoxic (nitrogen bubbling) conditions with gamma-rays from a 1,000-curie cobalt-60 source. The dose-rate was approximately 300 krads/hr. Surface plate counts on 'Oxoid' nutrient agar were made before and after irradiation, and the colonies were counted after 48 hr. incubation at 30° C.

The survival curves in the presence and absence of 0·001 *M* N-ethylmaleimide are shown in Fig. 1, and it can be seen that a pronounced sensitization occurred. Under nitrogen there was approximately a two-fold difference in the sensitivity of control and treated cells, although under air sensitization was not so marked especially at the lower levels of irradiation. Incubation with 0·001 *M* N-ethylmaleimide for a period of 20 min. immediately after irradiation did not enhance radiation damage, nor was it toxic to unirradiated cells at this concentration, indicating that it is a true sensitizing agent. The shape of the aerobic curve suggested that pre-incubation with the sensitizing agent for several minutes might be necessary for the attainment of the full effect (under nitrogen there was always 6 min. incubation before irradiation while oxygen was removed). Various times of pre-incubation were therefore tried, and it was found that a definite sensitization was observed with pre-incubation for as little as 1 min. The full effect was attained within 5 min. and there was no increase in sensitization when the pre-incubation period was increased from 5 to 15 min.

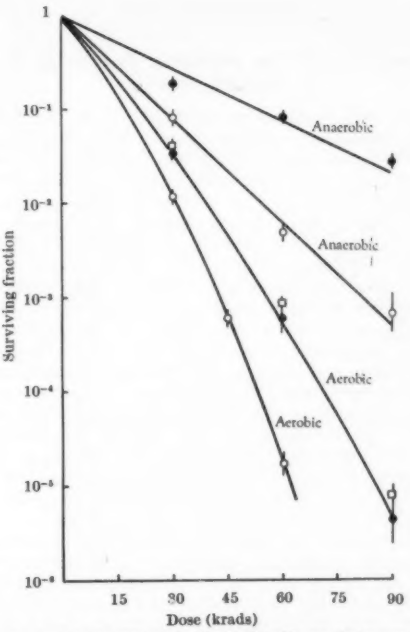

Fig. 1. Effect of 0·001 *M* N-ethylmaleimide on the inactivation of *Escherichia coli* strain *B/r* by gamma-radiation. ●, Control; ○, N-ethylmaleimide added before irradiation; □, N-ethylmaleimide added after irradiation for 20 min.

The sensitizing action of this compound might be due to its ability to combine with sulphydryl groups. Compounds with this property do not appear to have been reported before as sensitizers of bacteria to irradiation under controlled gas conditions, although halogen acetates which also combine with sulphydryl groups have been reported as sensitizing agents for mammals[1–3]. Kiga and his co-authors[4] reported that maleic acid enhanced the effect of X-rays on *Saccharomyces ellipsoideus*. If, however, the inhibitory action of maleic acid on respiratory enzymes influenced the concentration of dissolved oxygen, then the observed enhancement in this instance could be due to an effect of oxygen rather than to maleic acid directly. It may be significant that experiments in this Laboratory under controlled gas conditions have failed to show any sensitizing action of maleic acid on *E. coli* strain *B/r*.

I wish to thank Mr. M. J. Ashwood-Smith for discussions during the early part of this work.

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PHYSIOLOGY

Analysis of the Junction Potential of a Small Nerve

Fatt and Katz[1] demonstrated with the aid of an intracellular microelectrode that the end-plate potential was produced in the region of the motor end-plate by a sudden and transient reduction in the membrane potential as a result of neuromuscular transmitter action. They further pointed out that the prolonged decline of the end-plate potential was almost exponential and was determined by the electrical properties of the resting muscle membrane. An equivalent circuit of the resting muscle membrane is represented as a condenser in parallel with a battery (membrane potential) with a series resistance (membrane resistance). In the active phase of the end-plate potential, the membrane resistance at the junctional region is suddenly reduced by the transmitter action, that is, the muscle membrane is shortened by a shunting resistance[1]. To demonstrate the active process of the end-plate potential, Takeuchi and Takeuchi[2] and Oomura and Tomita[3,4] recorded a current flowing through the end-plate region of the muscle membrane by stimulating the nerve under conditions where the membrane potential was kept at the resting level, using the voltage-clamp technique[5,6]. On the other hand, the small motor nerve fibres which innervate the slow muscle fibres and relate to the tonic function in the maintenance of posture, also produce the junction potential of the small nerve at the junction region by its stimulation[7]. A distinctive feature of this junction potential is that it displays two phases with a terminal phase of hyperpolarization[7]. In the present work an attempt has been made to analyse the mechanism of production of the junction potential of the small nerve, using the voltage-clamp technique.

Two microelectrodes were inserted (within 50μ of each other) into a slow muscle fibre, one for recording the membrane potential and the other for passing current through the membrane. For the voltage-clamp experiment, a negative feedback amplifier system was connected to the microelectrodes to keep the membrane potential constant at the resting level. Junction potentials were evoked by selectively stimulating the small motor axons[8]. All experiments were carried out on isolated biceps muscles of bullfrogs (*Rana catesbiana*), in a cold room at 7° C. in summer.

The membrane potential of the resting slow muscle fibre ranged between 40 and 70 mV., the inside of the muscle being negative. In this experiment the time-constant of the resting muscle membrane, resistance multiplied by capacity, ranged from 500 to 1,000 m.sec. Occasionally after the insertion of the recording electrode at the region of the junction of the muscle a simple monophasic form of the small-nerve junction potential (see Figs. 1 and 2) was obtained. The time-course of the falling phase of this potential was roughly exponential, the $1/e$ decay time being approximately 800 m.sec. (note that this value is comparable with that of the time constant of the resting muscle membrane). The simple monophasic form soon (within 1 or 2 sec.) changed into the diphasic decay form (Fig. 3), which is characteristic of hyperpolarization, being accompanied by a 10 per cent reduction of the membrane potential. When the negativity of the membrane potential was increased by a steady inward current before applying a stimulation, the junction potential of the small nerve with the diphasic form (Fig. 3) changed to the monophasic form (Fig. 2). We therefore think that the small-nerve junction potential is of the monophasic form (Figs. 1 and 2), where the decline of the potential is determined by the electrical properties of the resting membrane as is the end-plate potential, and that the diphasic decay is due to a mechanism developed by injury of the muscle membrane at the junction region caused by impalement by the electrode.

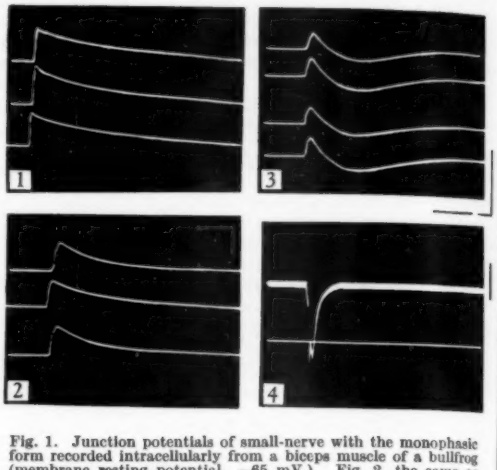

Fig. 1. Junction potentials of small-nerve with the monophasic form recorded intracellularly from a biceps muscle of a bullfrog (membrane resting potential, −65 mV.). Fig. 2, the same as 1, but from a different fibre (resting potential, −60 mV.). Fig. 3, junction potentials of small-nerve with a diphasic form (resting potential, −54 mV.). This characteristic form was changed from the monophasic one of Fig. 2. Upward deflexion shows the depolarization and downward one the hyperpolarization. Fig. 4, the current (upper oscilloscope tracing) obtained at the same junction from which Fig. 3 was taken under the clamped condition. The membrane potential was kept at the resting level (−54 mV.) as shown by the lower tracing. Calibrations are 40 mV. for potential, 2×10^{-6} amp. for current. Horizontal bar: 500 m.sec. Temperature, 7° C.

The current showing the active phase of the small-nerve junction potential of the small nerve was obtained by the voltage-clamp experiment. The upper tracing of Fig. 4 shows the clamped current flowing through the junction of the muscle at the same junction where the record in Fig. 3 was taken. This current was obtained by stimulating the nerve under the condition where the membrane potential was kept at the resting level, as shown by the lower oscilloscope tracing of Fig. 4. It declined monophasically with an almost exponential time course, although the small-nerve junction potential on Fig. 3 decayed diphasically, and the current corresponding to the phase of hyperpolarization of the junction potential was not shown in the current observed. The clamped current represents the active phase, that is, the temporal change of the shunting resistance across the muscle membrane at the junction region (similar to the case of the current obtained at the end-plate region). The time-course of the clamped current was not altered significantly by making the membrane potential more negative, while the time course of the small-nerve junction potential changed from the diphasic to the monophasic form.

The intensity and the time-course of the clamped current and the amplitude of the small-nerve junction potential were increased by adding a small amount

of tetraethylammonium chloride or eserine to the Ringer solution bath. However, the intensity of the clamped current was not altered by excess calcium ions, while the amplitude of the small-nerve junction potential was increased. Since the clamped current represents the active process at the junction region, increases of both potential and current may indicate an increase in the amount of the transmitter substance liberated and the prolongation of its action. The increase of the junction potential without increase of the clamped current may not involve these mechanisms, but may be due to the increase of the resistance of the resting muscle membrane by calcium.

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Cell Proliferation in Precancerous Liver: Linear Growth Curve

IN extending our recently published work on cell growth and the development of tumours[1], we have observed that in the livers of rats fed 2-acetylaminofluorene the cell proliferation continues at a constant rate during the pre-cancerous period and does not decrease as we had at first supposed. Such continuous increase in a cell population at a constant rate constitutes a most unusual form of growth, and it affords an important insight into the dynamics of cell proliferation in a pre-neoplastic tissue.

As in the previous experiments[1], male rats of the Holtzman and Sprague–Dawley strains were fed continuously a commercial grain diet containing 2-acetylaminofluorene. In several of our experiments we have measured the consumption of 2-acetylaminofluorene, and have found it to be quite constant throughout the experiment. Eight similar experiments have been carried out to date, involving a total of about 400 rats; from these experiments, one has been selected for presentation in Figs. 1–3. In this experiment the initial body-weight of the animals was 135 gm., and the concentration of 2-acetylaminofluorene in the diet was 0·06 per cent. For each experimental point, 4 rats were chosen with body-weights representative of the average and range of body-weights of the whole experimental group. They were killed with ether, and the livers were removed and perfused immediately. Then the livers were pressed through a plastic tissue mincer and the mince from 4 livers was mixed carefully; an aliquot of this mixed mince was then homogenized in 0·88 *M* sucrose. The nuclei were counted in a hæmacytometer after

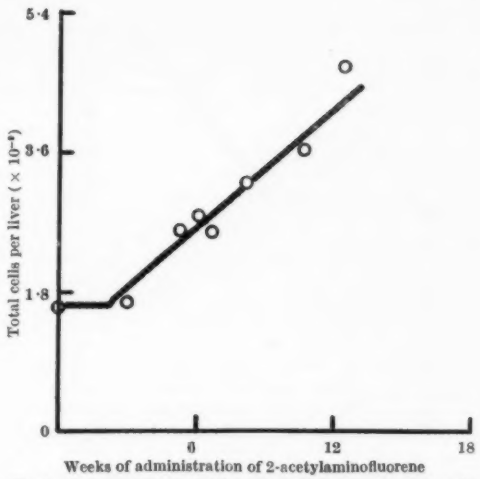

Fig. 1. Changes in the total number of liver cells during the continuous administration of 2-acetylaminofluorene in the diet

dilution of the sucrose homogenate 1 : 40 in 3 per cent acetic acid containing a nuclear stain; under these conditions the nuclei are well dispersed and easily counted. From the known concentration of liver in the homogenate and the known dilution of the homogenate in the counting fluid, the number of nuclei per gram of fresh liver and per whole liver was calculated. The protein nitrogen and nucleic acids of the homogenate were also determined[2,3], and the analytical results were expressed in terms of the average whole liver by multiplying the values obtained per gram by the fresh weight of the livers.

Fig. 1 shows the changes observed in the total number of liver cells. As we reported in our recent paper[1], the number of cells per average liver remained unchanged for several weeks after the administration of 2-acetylaminofluorene was started. Two of the experimental animals died during the fifth week of the experiment, in agreement with our previous findings[1]. The early period of cell constancy was followed by a rapid increase in the number of liver cells, with the result that by 12 weeks in this experiment the number of liver cells had increased about three-fold. The cell proliferation of this second period was essentially linear; the points fit well the straight line drawn through them by the method of least squares. The slope of the line is 0·268; this means that on the average 268×10^6 new cells were produced every week. This linear growth has been maintained in other experiments through the twenty-third week, or up to the time at which tumours were beginning to appear, and hence is characteristic of the entire pre-cancerous period.

Figs. 2 and 3 show the corresponding changes in the protein nitrogen and ribonucleic acid in the same livers. After an early period in which some loss of these biochemical constituents occurred, they also increased in a straight line. The protein nitrogen increased at a constant rate of about 28 mgm. per week, and the ribonucleic acid at a constant rate of about 9 mgm. per week.

It was an unexpected finding that the number of liver cells increased at a constant rate. However, this linear growth has now been demonstrated in all of a current total of 8 different groups of experimental animals. Cell proliferation at a constant, and thus

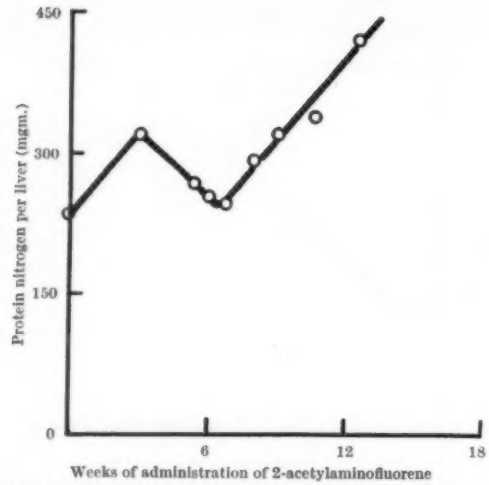

Fig. 2. Changes in the total quantity of protein nitrogen in the liver during the continuous administration of 2-acetylaminofluorene in the diet

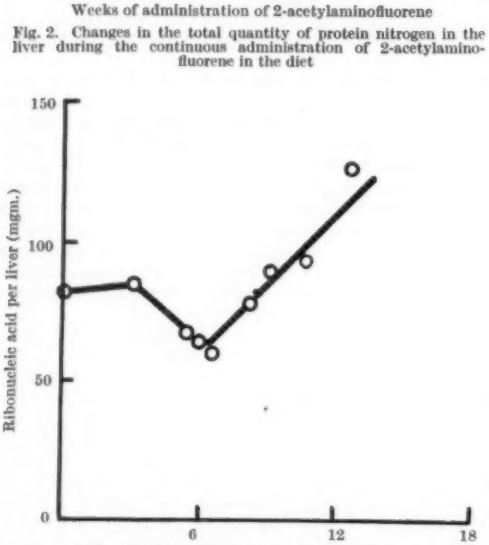

Fig. 3. Changes in the total quantity of ribonucleic acid in the liver during the continuous administration of 2-acetylaminofluorene in the diet

statistically linear-rate can be assumed to occur normally in such tissues as intestinal epithelium and the blood-forming organs, where the total population remains essentially constant over long periods of time. In these tissues cell proliferation is not autonomous, but is under the control of regulatory mechanisms in the animal that assure the delicate compensatory adjustment of the production of new cells to the constant loss of mature cells from the system. The linear cell proliferation produced in the liver by 2-acetylaminofluorene is probably a compensatory phenomenon also. However, it cannot be compensatory to a loss of cells since the number of cells is actually increasing, and there is no evidence at any time of extensive necrosis in these livers[4,5]. This proliferation of liver cells might, however, be compensating a loss of some functional capacity of the liver that is inactivated or destroyed by 2-acetylaminofluorene and that is essential to the survival of the animal (usually a few of the animals die at the time the cell proliferation starts in the survivors[1]). The latent period preceding the onset of cell proliferation is to be expected if the functional capacity involved is normally present in an amount greater than the minimum necessary for survival. Although the exact mechanism is not understood at present, it is evident that the administration of 2-acetylaminofluorene in the diet at a constant rate produces a proliferation of liver cells at a constant rate, and it appears therefore that this cell proliferation represents a quantitative response to the amount of 2-acetylaminofluorene actually being consumed.

The relation of the large-scale proliferation of liver cells to the production of the few successful malignant cells which ultimately become tumours remains to be explained.

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Acetate Tolerance in the Young Lamb

Recent work has shown that alterations can be produced in the tolerance to acetate and glucose in adult sheep by varying the nature of the diet[1,2]. With the inclusion of maize in a diet of lucerne and wheaten chaff the response of an adult sheep to an intravenous injection of glucose or acetate simulates much more closely the rapid rate of removal of these substances from the vascular system characteristic of a monogastric animal[1].

There are now many observations on the glucose tolerance[3,4], insulin sensitivity[5], hexokinase activity[6], and blood volatile fatty acids[7] in sheep and lambs which indicate that many aspects of the metabolism of carbohydrate in young lambs differ from those of adult sheep.

In view of these observations, the response to injected acetate in the very young lamb was determined and followed at intervals for a period of four months after birth. Five Merino wether lambs running with their dams on a mixed pasture were used. At intervals of a few days an injection of acetic acid neutralized to *p*H 7·0 with sodium hydroxide (5 m.moles acetic/kgm. body-weight) was given into the jugular vein and samples of blood obtained at 2, 15, 30 and 60 min. after the injection. The concentration of total volatile fatty acid was determined in each sample and also in urine collected over several hours by attaching a small rubber bag to the abdomen of the animal.

The results from two of the lambs, typical of the whole series, are presented in Table 1 and clearly indicate that the new-born lamb can very rapidly remove injected acetate from the blood stream. Analyses made on blood taken before the acetate injection showed a concentration of volatile fatty acid within the range 0·2–0·6 m.mole/l. for lambs of all ages; this range has also been observed for adult sheep feeding on green pasture.

Table 1. CONCENTRATION OF VOLATILE FATTY ACIDS IN BLOOD (m.moles/l.) AFTER THE INJECTION OF ACETATE (5 m.moles/kgm.)

Age	Lamb No. 18			Lamb No. 21		
	Min. after acetate injection			Min. after acetate injection		
	2	15	30	2	15	30
1–2 days	8·26	3·32	0·08	8·05	3·24	0·48
6–7 days	8·46	2·32	0·06	9·14	3·31	0·20
2–3 weeks	11·16	2·45	0·37	9·00	2·09	0·44
4–6 weeks	10·58	4·43	0·66	10·06	4·42	0·39
10–12 weeks	11·16	4·57	1·08	11·44	6·51	2·03
14–16 weeks	13·66	6·48	3·97	12·95	5·91	3·60
Adult	21·63	10·13	4·36	20·43	7·00	3·97

During the first four weeks of life all injected acetate was removed from the blood by the end of 30 min. whereas with older lambs and adult sheep a period of up to 60 min. was observed before the pre-injection level was reached. That this rapid rate of removal in the young lamb was not associated with a low renal threshold was indicated by the very small excretion of acetate during a 6-hr. period following the acetate injection (1–2 m.moles or less than 4 per cent of the injected dose).

It is thus apparent that as the lamb becomes older its tolerance to acetate alters until at approximately four months of age the rate of disappearance of injected acetate is similar to that of the adult sheep. This gradual change is comparable with the change which takes place in glucose tolerance and insulin sensitivity. Some other parameters, however, such as alterations in hexokinase activity[6] and liver coenzyme *A*-levels[8], change much more rapidly and at an earlier age.

These observations are of interest in that they add further support to the hypothesis that the young lamb behaves in many respects like a non-ruminant, and only gradually develops some of the metabolic characteristics of the adult sheep.

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Hydrothermal Denaturation of Collagen

In a recent communication by Rigby and Spikes[1], structural breakdown of collagen is considered to be possible on its prolonged contact with water at a temperature as low as 40° C. Such alterations of human collagen are believed to be involved in the manifestation of rheumatic symptoms. Evidently, the authors are not aware of the fact that experimental evidence for the occurrence of gradual shrinkage and labilization of mammalian collagen in water at a temperature of 40–45° C. is on record. In the monograph[2] to which the authors refer in connexion with the correlation of hydroxyproline content of various collagens and their temperature of instantaneous shrinkage, T_S, work is cited[3] proving the rupture of intermolecular hydrogen bridges of collagen in the temperature-range mentioned (denaturation). Table 16 in the accompanying monograph[4] supplies substantiation. Hence, the speculative feature of their premise is removed.

By immersion of pieces of calf-skin (middle layer of corium) in water, covered with toluene, at 45° C. for one week, some 8 per cent of the protein was solubilized. The T_S of the corium was lowered from 67° C. to 56° C. The trypsin treatment (for method, see ref. 5) of the original corium resulted in 0·2 per cent degradation, whereas the corresponding figure for the corium treated with warm water was about 10 per cent. These findings indicate a marked labilization of the collagen on prolonged action of water at 45° C.

The main evidence referred to[2–4] was obtained by a method which was devised by me and applied in an extensive series of investigations of the effect of denaturation of collagen, by hydrogen-bond breakers and hydrothermal forces, on its reactivity and properties[6]. It relies on the fact that, by denaturation of the skin protein, its hydrogen-bonding capacity is drastically increased. However, its affinity for agents which react with the protein by electrovalent forces exclusively is not altered. Such agents are 0·1 *N* hydrochloric acid and cationic chromium complexes[6], indicating the non-participation of ionic protein groups in this denaturation. For chromium complexes of high degree of aggregation, partly in the non-ionic state (extremely basic chlorides and perchlorates, as well as sulphito-chromium-sulphates), the keto-imide groups serve as the chief binding sites. By breaking or rupture of the hydrogen bridges between adjacent keto-imide groups, resulting from steric effects induced by the shrinkage of the collagen, new binding sites on these uncompensated groups, and possibly on some hydroxy groups, are made available for reaction. Thus, corium which had undergone pretreatment in water at 45° C. fixed 7·4 m.equivalents of chromium per gm. of collagen irreversibly from a solution of 33 per cent acid chromium perchlorate[7], while original collagen combined with 5·1 m.equivalents of chromium only. For the sulphito-chromium sulphate[8], the corresponding figures were 11·7 and 8·0.

Supporting evidence for the breaking of hydrogen bridges, by the unfavourable steric condition produced by the shrinkage of collagen, supplies data on the fixation of polyphenols (vegetable tannins), which for their main fixation by collagen depend on the function of the keto-imide groups as acceptors for hydrogen bonds donated by the phenolic groups[6,9]; one of the main pieces of evidence being their binding by polyamides[9]. In the present instance, with mimosa bark tannins at a final *p*H of 5·0, the collagen treated with warm water fixed 87 per cent of its weight of these tannins irreversibly, while the original collagen combined with 66 per cent of tannins.

These results prove the occurrence of marked disorganization and impaired stability of the skin protein by water at 45° C., or at a temperature some 25° C. below the normal T_S of mammalian corium. This gradual shrinkage differs only in degree from the instantaneous shrinkage; for example, in alterations in stability and reactivity of the collagen. In

the present example, about 40 per cent of the maximum effect of the augmentation of the co-ordination potency due to complete shrinkage of collagen resulted.

These investigations were carried out at a time when the present, simple but powerful, techniques in protein chemistry were not available. Then, the nature of the degradation products could not be investigated. In the light of recent findings, polypeptides containing a disproportionately large amount of hydroxyproline residues are released on the shrinkage of *young* collagen[11]. The content of this important amino-acid should then be lowered by denaturation, conforming to the view of Rigby and Spikes[1]—a fact apparently of importance for their main problem. References given in footnote 11 should be noted in this context.

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We are pleased to find that Prof. Gustavson has further chemical evidence which supports our speculations. We were aware of the references[1,2] listed by Prof. Gustavson when referring to the gradual shrinkage of collagen at temperatures below the instantaneous shrinkage temperature. However, we took these observations to be complementary to the physical experiments of Weir[3], which show the 'rate process' nature of the shrinkage phenomenon and to which we did refer.

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PATHOLOGY

Carcinogenic Action of Diazomethane and of Nitroso-N-methyl Urethane

The transformation of inactive or slightly active compounds into effective carcinogens by O-methylation has been discussed previously[1], and it was suggested that endogenous carcinogens may possibly be formed by alkylation of normal cell constituents in the body. Such a mechanism could account also for the carcinogenic effects of radiation and of remotely acting agents, such as the azo-dyes, ethionine, etc., which may give rise to alkyl radicals in the body.

Fig. 1. Lung of an *A/2G* male mouse that died after 11·5 months of application of etheral diazomethane to the skin, showing one large and one small adenomata. (× 3)

To test this hypothesis, diazomethane was chosen as a suitable alkylating agent. It is able to effect methylation under physiological conditions of *p*H and temperature, evolving nitrogen as the only other product. Diazomethane is a gas and is usually obtained in etheral solutions by the decomposition with alkali of some nitroso-N-methyl compounds[2]. Such compounds may possibly give rise to diazomethane or methylene radicals enzymatically in the animal body, without the need of alkali and drastic conditions. The commercially available nitroso-N-methyl-urethane was used for the preparation of diazomethane, and was itself tested for carcinogenic activity.

The results of the exploratory experiments proved sufficiently encouraging to warrant reporting at the present stage.

Male mice and rats, 1–3 months old, were used. Mice of the *A/2G* strain were obtained from the Laboratory Animals Centre, Carshalton; Swiss albino mice were obtained from the National Institute for Medical Research, Mill Hill; rats were Wistar, bred locally from the Porton strain. All the animals were housed in metal cages and given the Medical Research Council diet 41*B* and water *ad libitum*.

Diazomethane was prepared according to Bachmann *et al.*[3]. Its etheral solutions were kept at − 5° C. for periods up to three months, and the concentration, estimated by the benzoic acid method, varied between 3·3 and 0·1 mgm./ml. The etheral solution was applied from a dropping pipette to the shaved skin of the interscapular region of twelve *A/2G* mice, five times weekly. Eight mice survived more than five months of such treatment, but all these died within twelve months with lung adenomata, often multiple and of considerable size (Fig. 1). No abnormalities were present on the skin at the site of application, possibly because of the protective action of keratin.

The effect of inhalation of diazomethane was then examined using twelve *A/2G* and six Swiss mice, and six Wistar rats. For this purpose the animals were placed in a desiccator, 6,250 ml. capacity (in groups comprising six mice or two to three rats at a time) and 1 ml. of etheral diazomethane solution was

introduced from a syringe through a plastic cover replacing the stopper in the lid. Control animals (twelve mice of the *A/2G* strain and six Swiss mice, and two Wistar rats) were similarly exposed to ether only. The times of exposure were 1 or 2 min., twice weekly, for six months. When an animal appeared in poor condition, its treatment was terminated earlier. All the animals exposed to diazomethane by inhalation developed lung lesions, some dying acutely of lung œdema. Those dying later all had lungs grossly deformed, nodular and brownish.

All the mice of *A/2G* strain died within seven and a half months, and the majority had lung adenomata. Mice of the *A/2G* strain develop spontaneous lung adenomata in old age. However, in *A/2G* mice treated with diazomethane the incidence of these tumours was greatly accelerated. Only one or two small adenomata were found in the control *A/2G* mice killed at comparable age. Shimkin and Lorenz[4] observed similar acceleration of the development of adenomata in mice of the *A* strain injected intravenously with carcinogenic polycyclic hydrocarbons, and considered this as evidence of carcinogenic activity for the lung.

The lesions in the Wistar rats and in the Swiss mice affected mainly the bronchii. These became more prominent with time. Animals were killed at intervals even when still in good condition, in order to observe the evolution of the lesions. The last mouse and the last rat were killed eleven months after the beginning of treatment and about 5 months after its termination. The rat had a whitish big cellular tumour 2–3 cm. diameter in the right lobe of the lung, adhering to the chest wall. All the other lobes of the lung were studded with smaller whitish nodules, 1–5 mm. in diameter. Similar whitish nodules covered, and adhered to, the inner surface of the chest; they were particularly numerous at the upper right side and on the diaphragm. The organs in the peritoneal cavity did not appear grossly infiltrated by the tumour. Microscopically, the tumour and the disseminated nodules proved to be a carcinoma of the bronchial epithelium containing many mitotic figures. The control Swiss mice and Wistar rats, which were exposed to ether only, did not show any significant abnormalities when killed at the time of death of the last experimental animals.

Nitroso-N-methyl urethane was administered orally to Wistar rats. A single dose of 0·1–0·2 ml. of a 20 per cent or 2·5 per cent solution in 50 per cent or 5 per cent aqueous alcohol, respectively, was given by stomach tube to two groups of 10 and 6 rats respectively. The animals were then left without further treatment. The rats which received the 20 per cent solution all died within two to three days. Their lungs were dark red, some showed subcutaneous œdema, they had enlarged pale livers, and all had stomachs distended with fluid content, often containing blood, and hæmorrhagic petechiæ were present on the stomach walls. Microscopically, the livers showed necrosis confined to the portal areas, and the lungs, perivascular and peribronchial œdema and hæmorrhage into the alveoli.

Rats which were given the lower dosage survived from 10 days to 20 months. Their livers appeared normal, and lesions, if any, were confined to their stomachs and lungs. One of the rats which died 19 months after a single dose of the compound had a large, irregular, whitish mass in the abdominal cavity, involving the stomach, small intestines and spleen. There were also numerous nodules spread throughout the peritoneal cavity. Unfortunately, there was severe postmortem change, but microscopic examination indicated squamous carcinoma of the stomach with peritoneal spread (Figs. 2 and 3).

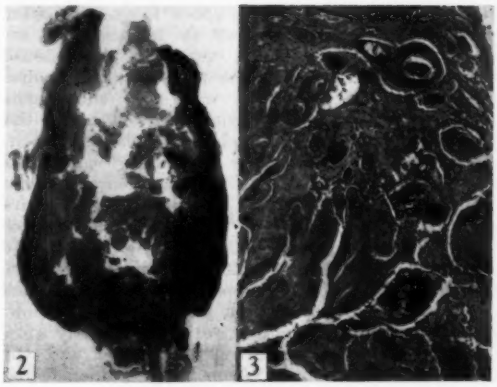

Fig. 2. Stomach of a male rat that died 19 months after a single oral dose (50 mgm./kgm. body-weight) of nitroso-N-methyl-urethane. (× 1·5)

Fig. 3. The same rat as Fig. 2, section showing squamous carcinoma of the fore-stomach. Hæmatoxylin and eosin. (×37·5)

In our colony no stomach tumours have been seen at autopsy of several thousand treated and untreated rats. There was also no reason to suspect vitamin A deficiency, therefore the stomach tumour was probably caused by nitroso-N-methyl-urethane.

I am grateful to Dr. P. N. Magee for the microscopic evaluation of the various lesions, which will be described in detail elsewhere, and to Dr. J. M. Barnes for his interest. I also thank Mr. M. R. Greenwood for valuable technical assistance, and Mr. R. F. Legg for the photographs.

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Serum Protein Abnormalities in 'Runted' Albino Rats

In the course of previous investigations, we have observed that when either normal or neoplastic tissues of mouse origin are injected into new-born albino *CFN* rats (Carworth–Wistar origin) occasional animals will develop a wasting disease characterized by roughened scaly skin, sparse hair growth, failure to gain weight normally, and sometimes actual loss of weight[1,2]. This condition usually appears during the first 7–14 days of life and many of the animals so afflicted succumb within a few days. Others survive this crisis and live for at least 35 days. Apart from the sparse hair and stunted growth, these survivors are apparently normal.

The same phenomenon is occasionally observed following intraperitoneal inoculation of normal adult *DBA/2* mouse spleen cells into new-born albino

rats[1]; but it occurs much more frequently after subcutaneous, intraperitoneal[2] or intracerebral injection of one of several transplantable mouse tumours into this host. The transplantable mouse tumours so far associated with this subsequent wasting disease are the Ehrlich ascites tumour, the lymphoma *L*4946, the lymphoma *P*1534, the lymphosarcoma *6C3HED*, the mammary carcinoma *BW*10232, the melanoma *S*91 and the neuroblastoma *C*1300. Many of the young rats appeared to expire as a direct result of the growth of the Ehrlich ascites tumour, the lymphoma *P*1534, the lymphoma *L*4946 and the lymphosarcoma 6C3*HED*; but there were individuals in which the wasting condition became evident during or after tumour regression. Furthermore, this disorder occurred rather frequently after inoculation of the mammary carcinoma and the melanoma, neither of which ever demonstrated palpable growth.

This 'runted' rat is interesting because it is grossly similar to the runts described in homologous transplantation studies[3–5]. Autopsied rats dying with this disorder reveal some of the general characteristics noted by Billingham and Brent[3]; the spleen is small, the thymus absent or quite small, the mesenteric lymph node usually absent and lymphogenous tissue generally reduced. When we exclude from consideration those rats appearing under-developed at birth or those which were survivors of litters having a high mortality during the first few days of life, only 6 animals which might be grossly classified as runts have been encountered in 251 rats injected with control Tyrode solution or not injected at all. Unfortunately, these animals were not autopsied, since the significance of this condition had not then been realized. In contrast, 15 of 23 rats inoculated at birth with the mammary carcinoma *BW*10232 developed the runting disease.

Since it is probable that other abnormalities of the reticulo-endothelial system are present in the runted animals, we have begun an intensive investigation of the serum proteins. So far this investigation is limited to those animals surviving the first 5 weeks of life. At this age, normal litter mates raised under identical conditions weigh 75–100 gm., whereas the runts weigh 35–55 gm. This communication constitutes a preliminary report on the serum protein fractions in these animals.

Tissue suspensions of mouse melanoma *S*91, mammary carcinoma *BW*10232, and normal *DBA*/2 spleens were prepared by mincing with fine dissecting scissors followed by gentle manipulation in a glass homogenizer to which Tyrode solution had been added. New-born *CFN* rats were injected with approximately 20×10^6 cells from one of these suspensions. The normal spleen cells were administered intraperitoneally, whereas the tumour cells were injected subcutaneously. Control groups of rats having received either 0·1 ml. of Tyrode solution or no injection at all were included. The animals were inspected at intervals of 2–4 days and were weighed each week.

Following the weighing at 5 weeks of age, blood was drawn by cardiac puncture, the serum collected and paper electrophoresis of the serum proteins carried out with a Spinco model *RB* electrophoresis apparatus. Serum aliquots of 0·008 ml. were subjected to electrophoresis at 4·0 m.amp./cell for 18 hr. at room temperature. The strips were dried, stained, and analysed with a Model *RB* analytrol.

Table 1. Serum Protein Fractions in 5-week-old Normal and 'Runted' Albino Rats injected at Birth with Mouse Tissues

Material injected at birth	No. tested	Mean weight (gm.)	Serum protein fraction			
			Albumin (per cent)	α_1- and α_2- (per cent)	β- (per cent)	γ- (per cent)
None	15	88	60·6	20·8	14·7	3·9
Tyrode solution*	9	90	60·2	20·9	14·6	4·3
Adult mouse spleen†	6	84	58·2	21·7	15·8	4·3
Mammary carcinoma‡	3	89	60·5	20·0	14·8	4·7
Melanoma§	4	88	61·9	20·8	14·0	3·3
Adult mouse spleen†	7	45	45·0	20·3	21·0	13·7
Mammary carcinoma‡	3	31	48·1	20·6	18·6	12·7
Melanoma§	3	42	48·7	21·4	16·9	13·0

* Tyrode solution is utilized in preparation of the cell suspensions.
† Obtained from 12- to 16-week-old *DBA*/2 female mice.
‡ Mammary carcinoma, *BW*10232 indigenous to the *C*57*BL*/6 strain of mice.
§ Melanoma *S*91 indigenous to the *DBA*/2 strain of mice.

The serum protein fractions are indicated in Table 1. It can be seen that the β- and particularly the γ-globulins are elevated in those rats with subnormal weight. As Figs. 1 and 2 further indicate, the correlation is not with the kind of tissue injected at birth, but rather with the fact that a runt was produced by 5 weeks of age. For example, approximately 20×10^6 normal adult *DBA*/2 mouse spleen cells were injected intraperitoneally at birth into two rats, yet, as shown in Fig. 1, only the runt had an increased percentage of β- and γ-globulins. Furthermore, when melanoma *S*91 cells were inoculated subcutaneously into another pair as illustrated in Fig. 2, the increased globulin percentages were produced in the runt, but not in the normal animals.

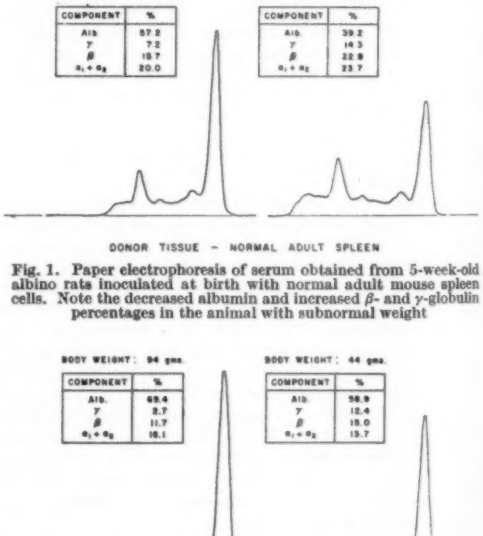

Fig. 1. Paper electrophoresis of serum obtained from 5-week-old albino rats inoculated at birth with normal adult mouse spleen cells. Note the decreased albumin and increased β- and γ-globulin percentages in the animal with subnormal weight

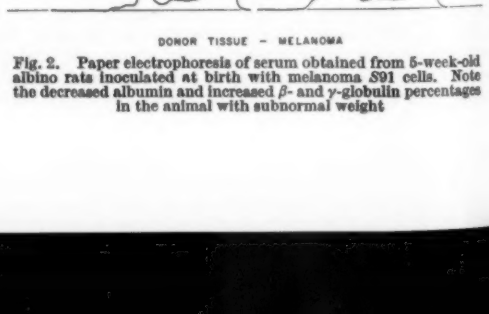

Fig. 2. Paper electrophoresis of serum obtained from 5-week-old albino rats inoculated at birth with melanoma *S*91 cells. Note the decreased albumin and increased β- and γ-globulin percentages in the animal with subnormal weight

The 6 untreated animals that died with the gross characteristics of wasting prevent us from concluding with certainty that the wasting disease in the young albino rat is directly attributable to the injection of normal or neoplastic mouse cells. We share with Billingham and Silvers[4] the opinion that in some instances the effect of this inoculation may rather be to aggravate or enhance another, as yet unrecognized, factor. These authors, moreover, have described a runted rat which follows the injection of homologous adult rat spleen or bone marrow cells. The most obvious feature of the homologous disease so produced was a severe dermatitis. Anderson *et al.*[5], however, have described runt disease produced by the intravenous injection of homologous thoracic duct lymphocytes into albino rats without reporting any skin involvement. We have not observed severe dermatitis in the runt disease of our albino rats following the inoculation of heterologous mouse tissues. Although the explanation of these discrepancies may lie in the fact that different strains of rats are utilized by each group, we must consider the possibility that different etiological mechanisms are operating in the three experimental systems. Nevertheless, our results indicate that whatever the etiology of the runt encountered in our work, the production of an unusually high percentage of γ- and β-globulins results.

Of particular interest is the recent work of Gengozian[6], who reports a consistent elevation in the lipoproteins (γ- and β-globulins) in the radiation-induced rat-to-mouse chimera. This abnormally high fraction seems to be produced by the mouse host and not by the donor rat tissues. Using similar techniques, we intend to measure quantitative changes in proteins with the view of determining directly whether the higher percentages of β- and γ-globulins observed by us are of host rat or donor mouse origin.

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BIOLOGY

Occurrence and Distribution of Cytochrome $a + a_3$ in Plant Cells

CYTOCHROME *a* occurs in plant materials only in very low concentrations and its activity is rapidly lost in homogenates kept at room temperature. Numerous visual observations of its presumed α-band have nevertheless been recorded for a variety of plant materials[1–5]. The reported values have a rather wide scatter lying between $\lambda = 600$ and 605 mμ. Recently, cytochrome *a* has also been recorded spectrophotometrically, but still with an equally wide scatter of the position of the α-band[6–10]. Observations tending to show the presence of the a_3 compound in plant materials have so far been very few.

Embryos of wheat appear to contain relatively large amounts of cytochrome *a* and its α-band appears stronger in comparison with the α-bands of cytochromes *b* and *c* than is usual in visual low-dispersion spectra. The spectrum is best observed in a mitochondrial pellet of the consistency of a thick paste.

Mitochondria were extracted by conventional methods from viable wheat germ freed from endosperm particles by flotation on a mixture of cyclohexane and carbon tetrachloride (10 : 25 v/v). The mitochondrial pellet was finally centrifuged down at 10,000*g* from a medium containing 0·2 *M* sucrose, 0·05 *M* phosphate *p*H 7·2 and 0·001 *M* magnesium sulphate, and examined in a layer about 10 mm. deep with a Beck microspectroscope. After reduction with sodium ascorbate a well-defined absorption band was visible at $\lambda = 600$ mμ and another at 552 mμ. They were still visible after 24 hr. in a deep freeze when again reduced with dithionite. After each reduction the cuvette containing the pellet was flushed out with carbon monoxide and the spectrum re-examined shortly after. The band at 600 mμ moved to 590–592 mμ, while that at 552 mμ remained unaltered.

Attempts to confirm these observations with a spectrophotometer were at first frustrated by the very high degree of light scatter caused by the mitochondria in suspension. Even after addition of 0·025 gm. cytochrome *c* to 3·0 ml. of mitochondrial suspension no definite absorption band was recorded. Effective observation was achieved by the following method using a Unicam *SP* 500 spectrophotometer with a *SZG* 500 photomultiplier attachment. The mitochondria were re-suspended in the sucrose-phosphate medium and subjected to ultrasonic vibration (5,000 cycles per min.) for 20 min. and then centrifuged down at 100,000*g* for 30 min. The pellet was re-suspended in 2 ml. of 60 per cent glycerol + 40 per cent sucrose-phosphate medium. The cuvette containing the suspension was placed as close to the photomultiplier unit as the construction of the apparatus would allow (about 1 cm. distance) instead of in its normal position by the light slit. With these precautions absorption curves could be recorded between wave-lengths 580 mμ and 610 mμ. The continuous curve in Fig. 1 shows the difference in absorption by the mitochondrial suspension before and after reduction with a trace of dithionite. The usual α-peak is shown at 602 mμ and a secondary peak at 594 mμ due to reduced peroxidase[11]. After treatment with carbon monoxide the absorption-difference curve was changed to that shown by the broken line,

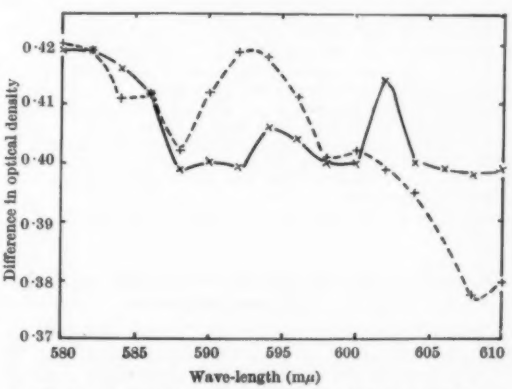

Fig. 1. —, no carbon monoxide; – –, plus carbon monoxide

revealing the formation of the cytochrome a_3–carbon monoxide compound with an absorption maximum at about 592 mμ. At the same time a corresponding change occurred in the deep blue region of the spectrum, a small peak appearing at 424–426 mμ, attributable to the γ-band of the cytochrome a_3–carbon monoxide compound.

Electronmicrographs of thin sections of the mitochondrial pellets treated with osmium tetroxide have been prepared for us by Dr. M. S. C. Birbeck. The mitochondria show the normal type of structure as seen in thin sections of tissue. Broken mitochondria and other detritus are rare. After vibration the walls and lamellæ were entirely broken down into a fairly uniform mass of particles with a mean diameter of about 30 mμ. Any soluble contents of the mitochondria would, of course, have been removed by the final centrifugation.

The above observations seem to make it clear that both components of the cytochrome $a + a_3$ complex are present in the cells of wheat embryos. Their spectra can only be clearly observed after the cell components other than mitochondria have been discarded, and no bands have been observed in the supernatant after the mitochondria have been removed. Disintegration of the mitochondria shows that the two components are both attached to the mitochondrial membranes and are not discarded with the internal fluids.

Repeated spectroscopic investigation of preparations of isolated nuclei from the same tissues have failed to reveal any bands attributable to any of the respiratory cytochromes. None was detectable in nuclear suspensions having twenty times as much total nitrogen as that required to give visible bands with mitochondria. The embryonic cells investigated did not contain chloroplasts; but it has already been shown that the chloroplasts of green cells do not contain any detectable cytochromes other than b_6 and f (refs. 12, 13). It appears probable that the cytochrome $a + a_3$ complex occurs in higher plant cells, as previously shown for others, only on the membranes of the mitochondria.

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A New Type of Citrus Fruit Rot caused by *P. italicum* Wehmer

During the past five years, while engaged on the examination of arrivals of Israeli citrus fruit in Britain and on the Continent, an unfamiliar type of dark red varying to bronze-red mould rot on oranges and grapefruit was occasionally found. So far as I am aware this rot has not been previously recorded.

Microscopic examination of the affected rind tissue revealed fungal penetration, and that many of the fungal cells within the tissue and on the rind surface had reddish pigmented contents. Sub-plants on common nutrient agar media invariably produced the blue mould fungus *Penicillium italicum*, yet it seemed inconceivable that the citrus blue mould rot fungus could be the causal organism of this new type of fruit rot.

The new fruit rot is of minor economic significance, as demonstrated in Table 1, which records the incidence of the rot as compared with the total fungal waste found in personally examined orange and grapefruit consignments in the four years 1957–60.

Table 1. Comparison of the Incidence of the Red Fruit Rot with the Total Fungal Waste seen in Fruit Consignments in the Years 1957–60

	1957	1958	1959	1960
No. of citrus fruits examined	128,228	226,270	218,030	100,553
Total number of rots	7,304	5,997	4,420	601
No. of red rots	36	34	93	18
Percentage of red rots to total rots	0·5	0·6	2·1	3·0

In a single instance a reddish-brown fungus was isolated in culture as well as *P. italicum*. The former organism was identified by Mr. E. W. Mason of the Commonwealth Institute of Mycology, Kew, as *Ascocybe grovesii* Wells, an unusual type of Ascomycete which was diagnosed, classified and recognized as a new organism by Doreen E. Wells, and given its nomenclature as recently as 1954. The organism is of common occurrence on lumber wood, causing a brown surface stain.

Oranges inoculated with the *Ascocybe* fungus developed a very slow rot, in initial stages reddish-brown in colour but turning dark brown with age, and the fungus was readily isolated from the induced rot.

Uncertain as to whether the single isolate of the *Ascocybe* fungus was of chance occurrence or indeed primarily responsible for the dark red citrus fruit rot and later retarded by the development of the common blue mould fungus, the influence of diphenyl on the growth of both organisms on common nutrient agar media at different *p*H levels was studied, with the view of applying the knowledge gained to further attempts on the isolation of the causal organism of the new fruit rot.

Diphenyl, a fungistat much used in the citrus industry, proved to have little influence on the *Ascocybe* fungus. The rate of growth of the fungus was in some instances somewhat reduced, but the fungal fructifications—the hyaline conidia, the erect brown ascophores and hyaline ascospores—and the production of a characteristic reddish-brown diffusible pigment, remained unaffected by the diphenyl.

The response of the blue mould fungus *P. italicum* to diphenyl was most extraordinary. Instead of the normal fasicular development of a blue conidial mat on the culture media plates, growth was strikingly arrested, and very small atypical, well-raised, furrowed colonies developed changing in colour from whitish to yellow-bronze to reddish-bronze, often with a relatively wide dark red peripheral zone.

Conidia formation was generally inhibited, at times atypical with coarse stunted conidiophores bearing very few sterigmata and very few conidia. Most of the hyphal cells in the pigmented zone had reddish pigmented contents.

Oranges wounded and inoculated with *P. italicum* and placed with diphenyl under a bell-jar under dry and moist conditions developed the common blue mould rot, but with diphenyl in closed screw-capped jars the rot developed slowly and instead of the typical blue mould rot, irregularly scattered fascicular growths appeared, changing in colour in irregular patterns from dirty white to yellow-bronze to reddish-bronze, and blood red patches were also formed. Inoculated oranges without diphenyl in closed jars developed normal blue mould rot. In short, inoculated oranges with diphenyl in closed jars had produced, under the conditions of the experiment, a rot similar to some of the rot samples which showed visible reddish fungal growth on the fruit rind found in fruit consignments from Israel.

Whether the lack of oxygen or the increased ratio of carbon dioxide in the air mixture, and other substances as ammonia gas can induce the same type of rot is under investigation. It should be noted that two oranges in ammonia-treated experimental fruit consignments from Israel in 1958 actually showed the new type of red rot.

Fuller details will be published elsewhere.

I wish to express my gratitude to Mr. Marcus J. Sieff, director of Marks and Spencer, Ltd., and also to Mr. Nathan Goldenberg, chief of Marks and Spencer's Food Development Department, for generously placing at my disposal all laboratory facilities at Marks and Spencer's Analytical Laboratory.

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Growth Requirements of Pome-Fruit Tissues

CORTICAL and pith tissue from apple fruitlets undergoing cell division and vascular tissue from more mature fruits have been grown in sterile culture[1]. In this communication further definition of the growth requirements of apple and other pome-fruit tissues is made.

Growth of pear and quince fruit tissues in sterile culture was obtained on media similar to those used for apple tissue culture. Disks of tissue (thickness × diameter, 1 mm. × 3·8 mm.) excised from the mid-cortex of immature pear (Packham's Late, 45 days from fertilization, weight 20 gm.) and quince (Van Deman, 66 days from fertilization, weight 20 gm.) fruits showed no growth on a modified White's medium (agar content 0·55 per cent). Addition of coconut milk was without effect but addition of 2,4-dichlorophenoxyacetic acid (2 p.p.m., resulting medium termed *A*) induced active growth involving cell division. Addition of coconut milk to *A* (final concentration 10 per cent by volume) further stimulated growth. These responses to coconut milk and 2,4-dichlorophenoxyacetic acid resemble those obtained with apple fruitlet tissue excised during the period of cell division.

The effect of kinetin on the growth of these tissues has also been studied. Kinetin and *l*-asparagine, when both added to medium *A*, stimulated markedly the growth of pear cortical tissue, the stimulation exceeding that of coconut milk. With quince cortex this stimulation was less marked, the response being less than that obtained with coconut milk. The influence of *l*-asparagine, kinetin and 2,4-dichlorophenoxyacetic acid on the growth of immature pear cortex is indicated in Table 1.

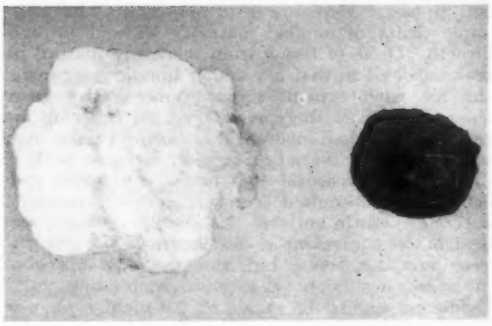

Fig. 1. Pear explants excised 45 days from fertilization after 34 days in culture. Right, explant which has shown negligible growth was cultured on medium *F*; left, on medium *E*

Table 1

Medium	Mean weight (mgm.) of explants after growth for 34 days
A (modified White's medium + 2,4-D 2 p.p.m.)	36
B (*A* + *l*-asparagine 180 p.p.m.)	67
C (*A* + *l*-asparagine − 2,4-D)	17
D (*A* + kinetin 0·1 p.p.m.)	46
E (*A* + *l*-asparagine + kinetin)	120
F (*A* + *l*-asparagine + kinetin − 2,4-D)	17

(*LSD* at 5 per cent level = 9, at 1 per cent = 12)

2,4-D = 2,4-dichlorophenoxyacetic acid.

Kinetin does not influence growth in the absence of 2,4-dichlorophenoxyacetic acid, stimulates only slightly in its presence, but stimulates appreciably in the presence of 2,4-dichlorophenoxyacetic acid + *l*-asparagine. Apple vascular tissue also responds to kinetin in the presence of 2,4-dichlorophenoxyacetic acid[1]. The growth effects of kinetin on other cultured tissues have all been observed in the presence of indole-3-acetic acid[2].

The rates of growth of pear cortical tissue on medium *E* and of quince on medium *A* + coconut milk were several times greater than those of apple vascular and fruitlet tissue on either of these media. Cultured pear and quince tissue is composed of very small cells, and percentage growth increment expressed on a cell-number basis is usually greater than that expressed on a fresh-weight basis.

Attempts have also been made to culture tissue from relatively mature pear and quince fruits. Only slight proliferation was obtained from pear cortical explants excised 113 days after fertilization and cultured on medium *A* supplemented with coconut milk, but more active growth was obtained from quince (variety Missouri Mammoth) cortical tissue excised 90–154 days from fertilization. Both 2,4-dichlorophenoxyacetic acid and coconut milk were needed to induce this proliferation. No information is available about the length of the period of cell division in pear and quince fruits, but it might be expected to be of short duration as in the apple. Since picking time for quince is about 170 days from fertilization, it is likely that with this fruit growth has been obtained from cortical tissue after the cessation of

cell division. Explants from mid-cortex and pith of apple fruits of similar maturity showed negligible growth. Disks of tissue from relatively mature pear fruits excised so that a vascular bundle ran centrally through each explant showed more active growth than tissue from the cortex, medium *E* giving more rapid growth than medium *A* + coconut milk. Apple vascular tissue (variety Sturmer) requires both 2,4-dichlorophenoxyacetic acid or an equivalent and a cell-division stimulant (coconut milk or kinetin) for active growth in culture[1]. 2,4-Dichlorophenoxyacetic acid or an equivalent is also essential for growth of pear vascular tissue, but this tissue is apparently much less dependent on a cell-division stimulant.

The possibility of replacing 2,4-dichlorophenoxyacetic acid by other compounds has been investigated. Apple and pear vascular tissue did not grow when 2,4-dichlorophenoxyacetic acid (1–5 p.p.m.) was replaced by indole-3-acetic acid (0·3–5 p.p.m.). Higher concentrations (30 p.p.m.) of indole-3-acetic acid produced some growth, but still considerably less than 2,4-dichlorophenoxyacetic acid. Potato-tuber tissue in the presence of coconut milk also shows this unusual dependence on 2,4-dichlorophenoxyacetic acid[2]. Quince cortex was more responsive to indole-3-acetic acid which, although relatively ineffective at 5 p.p.m. with this tissue, at 30 p.p.m. was nearly as effective as 2,4-dichlorophenoxyacetic acid (5 p.p.m.). For the growth of apple and pear vascular and quince cortical tissue, 2,4-dichlorophenoxyacetic acid can be replaced by some related phenoxy acids (for example, 2,4,5-trichlorophenoxypropionic acid).

Tissue has also been cultured from other pome fruits, namely, medlar (*Mespilus germanica* L.), Japanese quince (*Chaenomeles superba* Rehd.) and oriental pear (*Pyrus calleryana* Decne.).

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Protoplasts from *Penicillium glaucum*

Bachmann and Bonner[1] were able to obtain free protoplasts from *Neurospora crassa*, if this fungus was cultivated in thick liquid media, such as 20 per cent sucrose and 10 per cent enzyme preparations. Protoplasts emerge through pores in the hyphal walls. The authors showed, by means of a microscopical photo-series, that the protoplasts regenerate to form a complete new fungus mycelium.

If *Penicillium glaucum* was cultivated on thickened serum it was also possible to form protoplasts. Cells of the fungus were inoculated in thickened guinea pig serum between two sterilized glass plates and the upper glass bordered and fastened with paraffin. After some time (7–14 days) those upper plates were loosened, dried and stained with a May-Grünwald-Giemsa solution. (This simple method is very suitable for staining the internal structures of hyphæ in microscopical preparations.) Fig. 1 shows the connexion of the protoplasts with the 'vacuoles' of the interior structures of the hyphæ.

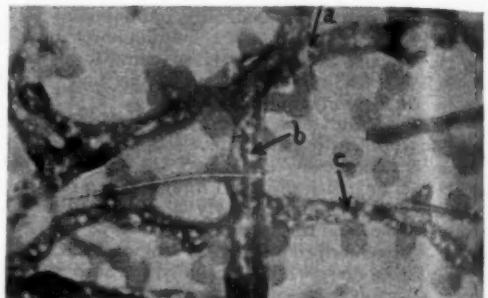

Fig. 1. Formation of protoplasts from *Penicillium glaucum* in a medium of thickened cell-free guinea pig serum. (× *c.* 1,500)

The photomicrograph shows reddish-grey, very tender forms between and on the blue hyphæ. Some of these forms are in direct connexion with the pores and 'vacuoles' of the hyphæ (*a*). Arrows *b* and *c* show these forms flowing out of the vacuoles.

In similar experiments with thick liquid media, such as sera and cell liquids, a wide extension of the hyphæ was observed. Here the typical internal structures of broad hyphæ found continues outside the hyphæ. They are embedded in complexes, the finest structures of which seem to move slowly into the surrounding medium without producing definite contours. The same effect could be seen if *Penicillium glaucum* was embedded into living plants. This, together with some photomicrographs, is published elsewhere[3].

Other experiments have been carried out on soft forms of protoplasts[3]. These results concerning the extension of internal structures may help towards understanding the above phenomenon[4].

In spite of the fact that these observations are different from the growth of fungi in normally used media, which regularly produce a quick and unrestricted growth, the present observed forms are unnatural. Under natural conditions there are many opportunities for fungi to move into living tissues or thick cell liquids and cause fermentation. Therefore it is necessary to pay attention to those alterations in the fungal elements, in order to prevent mistakes of diagnosis. Also for the sake of common biological examinations the study of changes of the cell elements, caused by alterations of the surroundings, is most important[4,5].

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ENTOMOLOGY

Food of Housefly Larvæ

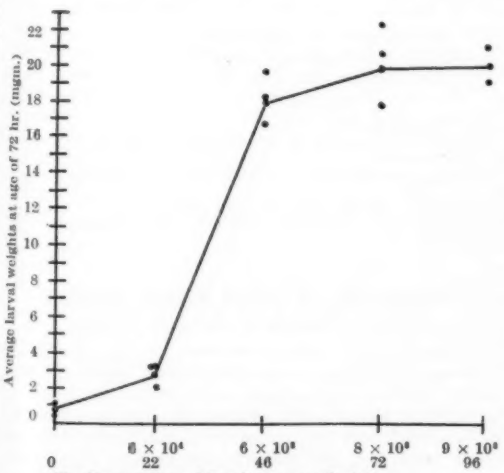
ALTHOUGH considerable information has been published on the nutritional requirements of fly larvæ (refs. 1–5 and Mer, G. G., personal communication) the actual natural food of these insects has never been unequivocally described. The biotopes of housefly larvæ consist of a variety of materials which by themselves appear nutritionally inadequate, but which have dense microbial floras (for example, animal excrements).

Culture methods for fly larvæ commonly used in laboratories require the addition of yeast to aqueous suspensions of either wheat bran, grass meal, oats or other similar materials[2]. Silverman and Silverman[3] replaced yeast by a controlled bacterial flora and achieved a more uniform growth of larvæ. In larvæ reared on this medium Mer (Mer, G. G., personal communication) found mainly bacterial cells in their foreguts. That living micro-organisms are not necessary for larval growth was shown by Greenberg[4]. He found that '*CSMA*' medium containing an uncontrolled microbial flora could be used, after being autoclaved, for culturing *M. domestica* under sterile conditions.

The aim of the present experiments was to clarify the larval relationship to *Escherichia coli*, which is the dominant micro-organism in breeding sites of housefly larvæ.

Newly hatched larvæ of *Musca vicina* Macq. were reared aseptically[5] for 3 days (to maximal body weight) at 35° C. at a density of one larva per gm. of experimental diets. These were mixtures of wheat bran (40 per cent), milk powder (2·5 per cent), and water (57·5 per cent) incubated for varied periods (Fig. 1) at 30° C. with approx. 4×10^4 *E. coli* (laboratory strain) per gram of medium, and autoclaved prior to use.

The results, which are summarized in Fig. 1, show that the wheat bran–milk suspension does not support larval growth when sterilized before substantial bacterial multiplication took place. This nutritional deficiency is, however, progressively



Top line, number of *E. coli* per gm. of mixture.
Bottom line, incubation period of mixture at 30° (hr.).

Fig. 1. Relationship between growth of *Musca* larvæ and concentration of *E. coli* in the wheat bran–milk mixture

Table 1. THE EFFECT OF FEEDING DRIED CELLS OF *E. coli* TO HOUSEFLY LARVÆ. 35 NEWLY HATCHED LARVÆ WERE USED PER EXPERIMENT

Amount of desiccated *E. coli* in diet (gm.)	(per cent)	No. of larvæ surviving at 72 hr.	Average larval weight at age of 72 hr. (mgm.)	No. of larvæ pupating	No. of flies hatching
0·3	1·2	0	—	—	—
0·6	2·3	13	1·4	0	—
1·25	4·8	33	10·8	18	11
2·50	9·1	32	20·6	31	28
3·40	12·0	35	21·0	33	32
Wheat bran–milk mixture containing 7×10^8 *E. coli*/gm.		32	18·9	31	29
Synthetic diet*		28	14·8	23	21

* This consists of vitamin-free casein 2·5 gm., cholesterol 0·025 gm., ribonucleic acid 0·025 gm., salt mixture No. 2 0·016 gm., 'Nipagin' *M* 0·07 gm., powdered filter paper 8·0 gm., water 17·5 gm.; and the following vitamins (μgm./gm. dry diet): thiamine 47, riboflavin 47, pyridoxine 38, pantothenic acid 95, nicotinic acid 238, folic acid 19, choline chloride 2,377, biotin 0·4, inositol 1,902, *p*-aminobenzoic acid 95, and vitamin B_{12} 0·2.

compensated by the accumulation of *E. coli* cells in the initial mixture. Larval growth was optimal when the bacterial concentration had increased to 8×10^8 per gram of diet, which corresponds to an approximately 9·6 per cent weight increase over that of the deficient initial medium. On diets containing the above or higher concentrations of *E. coli*, rates of pupation and adult emergence were comparable to values obtained on stock culture or natural housefly media.

To determine whether the nutritional value of *E. coli* is due to its cellular constituents or products of its metabolic activity, Seitz filtrates of the *E. coli* diets, supplemented with cholesterol (0·1 per cent) and adjusted to the texture of the initial mixture by addition of powdered filter paper, were prepared. Since these diets failed to support larval growth, it is evident that *E. coli* cells contain essential nutrients.

Washed *E. coli* were desiccated to constant weight, and were afterwards mixed in graded amounts (see Table 1) with portions of 25·0 ml. of water and 8·0 gm. of powdered filter paper (particle size <10 mesh) which had been previously impregnated with 0·05 gm. of cholesterol[5]. The texture of the diets resulting after autoclaving was as loose as that of media incubated with living bacteria. Thirty-five newly hatched larvæ were grown aseptically for 3 days on each of these diets.

The results of a typical experiment are summarized in Table 1. The growth-rate of *Musca* larvæ is obviously proportional to the dietary level of the dried bacteria and becomes optimal at concentrations (9·1–12·0 per cent) which closely resemble the weight addition of *E. coli* cells required to 'complete' the wheat bran–milk mixture. This indicates that, apart from cholesterol and water, *E. coli* cells are the only food derived by the larvæ from the above media.

When compared with a synthetic diet, the nutritional superiority of *E. coli* diets is striking. It should be recalled that dried *E. coli* contain 75 per cent of a protein which has a notably higher nutritional value for rats, chicks[6] and housefly larvæ[1] than conventional animal proteins. However, since cholesterol addition to the *E. coli* diet was indispensable for larval growth, the bacteria used appear to lack this constituent of animal cells.

One may conclude that the diverse materials on which housefly larvæ seem to thrive in Nature[7] are

merely substrates for bacteria, and these are most likely to be the actual food of the larvæ. It might be worth considering the use of desiccated *E. coli* with the above-mentioned supplements as a medium for standardized housefly rearing.

This work was carried out at the Medical Research Laboratories of the Medical Corps, Israel Defence Forces, during 1957.

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BACTERIOLOGY

Comaprison of Strains of *Streptomyces griseus* which produce Streptomycin and those which do not

We have examined a streptomycin-producing strain of *Streptomyces griseus*[1] and two mutants derived from it which did not produce streptomycin. The two mutants arose by treatment with mustard nitrogen[2]. They were isolated as a single colony by the method previously described[3]. Out of 1,387 *Streptomyces griseus* colonies grown from single spores after treatment with mustard nitrogen there appeared 33 non-producing colonies. Only two of them remained stable non-producers after being transferred several times. Their cultural and physiological characteristics differed from the parent strain.

After cultivation in media proposed by Waksman[4] they behaved as different species.

Comparing our strains on various sources of carbon, they proved to have different characteristics. They all grew on 1 per cent maltose, dextrose, pectin, amylum soluble, glycogen, *d*-ribose, xylose, *d*-fructose, mannose, *d*-galactose, dextrose, *l*-arabit, mannitol, glycerol, malate, succinate and fumarate, but did not grow, or very weakly so, on media containing 1 per cent saccharose, cellulose, inulin, rhamnose, sorbose, dulcit, inositol, acetate, tartarate, formate, pyruvate. Pronounced differences have been revealed on media containing arabinose and citrate (Table 1). One of the non-producing strains (No. 45) which was isolated first was not able to grow on citrate as the sole source of carbon. The inability to grow on citrate, however, was not connected with streptomycin production because the other non-producing strain (No. 20/52) was able to use this substrate in the same way as the parent strain did. The inability to make use of citrate was not connected with decreased permeability towards citrate. All three strains were able to decompose citrate. Citrate disappeared from the medium and oxygen consumption, measured in a Warburg apparatus, increased. (Citrate disappearance

Table 1. Carbohydrate Utilization by *Streptomyces griseus*

Carbon source	Parent strain *Streptomyces griseus*	Mutant strain No. 45	Mutant strain No. 20/52
Arabinose	♀	++++	++++
Citrate	+++	♀	+++

Inoculations were made by spore suspension on agar slopes, and results read on the fourteenth day of incubation.

was measured by chemical[5] determination of citrate in the supernatant, and by measuring the carbon-14-citrate isotope activity in the supernatant.)

The parent strain and mutant 20/52 consumed citrate with a lag phase of about 1 hr.; the other mutant without any lag phase promptly oxidized citrate and increased its Qo_2.

No metabolic block could occur in the two mutant strains in connexion with their inability to produce streptomycin, because both of them could synthetize their protoplasm from simple carbon sources and inorganic nitrogen sources.

There was, however, one striking difference between producing and non-producing mutant strains. The mutants in shaken culture grew only for a very short period of time. The young hyphæ branched very early in their development in every direction and they soon were packed together into spherical clumps, characterized by an almost homogeneous centre and short hyphæ protruding from it into the medium. These clumps grew in size, and spores were produced in very great numbers during the first 24 hr. of the culture. This mode of growth could be observed both in synthetic and complex organic media. It was not possible to achieve normal growth by changing the carbon–nitrogen ratio.

These results indicate that there exists some difference between streptomycin-producing and non-producing strains which lies in some fundamental metabolic change. Although the mutants were able to go through all important metabolic processes, they were not able to develop normally.

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Metabolism of Small Bodies isolated from a Stable *Proteus L* Form

Bacterial *L* forms consist of morphological elements of various sizes and shapes[1]. Many investigators of the *L* forms have paid special attention to granular bodies of a diameter of about 0·2μ, which are very often found in *L* cultures. According to Tulasne, these granules, or some of them, are viable and represent an important stage in the life-cycle of the *L* form[2]. This view has, however, been criticized by other workers[1,3].

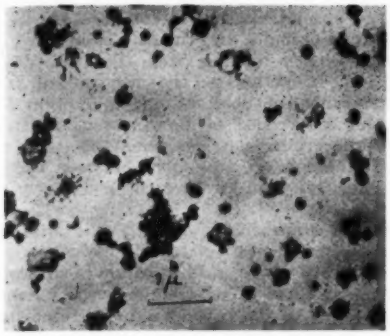

Fig. 1. Electron micrograph of small bodies isolated from a culture of *Proteus L9* by means of differential centrifugation

Separation of various morphological elements in an *L* culture by means of differential centrifugation has been described by Mandel *et al.*[4,5]. This technique has been applied in the present work. A stable *L* strain (*L9*) derived from *Proteus vulgaris*[6], was grown in a serum-free medium[7] and subjected to centrifugations at 5,500–78,000*g*. Thus fractions were obtained which essentially consisted of granules having a diameter of 0·1–0·3μ (Fig. 1).

The respiration of these granules, when suspended in the growth medium, was measured and compared with the respiration of the total culture. Table 1 gives the average values obtained from a number of experiments of this kind. It can be seen that the respiration of the small *L* granules is of the same order of magnitude as that of unfractionated *L* cultures. *L* bodies mechanically disintegrated for 5 min. in a Mickle disintegrator show at the most a very low respiration.

Table 1. Average Values of Respiration-Rates exhibited by *L* Bodies as measured by the Warburg Technique. The *L* Bodies were suspended in the Growth Medium

	Small granules	Total cultures	Total culture after mechanical disintegration
Q_{O_2}	200	402	< 5

The change in the nucleic acid content of the granules and the incorporation of phosphorus-32 into these bodies during 2–4 hr. incubation in the growth medium were also studied. The nucleic acid content remained approximately constant or decreased somewhat. The incorporation of phosphorus-32 in the nucleic acid fraction of the granules (prepared by the Schneider procedure) corresponded to less than 0·2 per cent of the nucleic acid content of these bodies. Under similar conditions, the nucleic acid content of whole *Proteus L9* cultures increased 2–3 times. Therefore, the possibility that the small amount of phosphorus-32 incorporated into the granular fraction could be attributed to contaminating *L* bodies of larger sizes cannot be excluded. Similarly, no significant incorporation of phosphorus-32 into the protein and lipid fractions of the small *L* granules could be ascertained.

The ribonucleic acid-content of the granules was found to be about the same (about 4 per cent) as that of unfractionated *L* bodies. The deoxyribonucleic acid content varied considerably and was often remarkably low (cf. Mandel *et al.*[5]).

The specific activities of the enzymes, succinic dehydrogenase and catalase, in the granules were found to be comparable to those of *L* bodies present in unfractionated cultures.

The experiments which have been described indicate that, under the prevailing conditions, the biosynthetic capabilities of the *L* granules studied are at the most very low compared to unfractionated *L* cultures. The high respiratory power of the granules is, however, worth emphasizing. Mandel *et al.*[4] reported that the small *L* bodies isolated by them from *Proteus P18* cultures did not degrade glucose aerobically. In these experiments, however, the *L* granules were not suspended in the growth medium, but in a Krebs medium. We have found that neither fractionated nor unfractionated *Proteus L9* bodies respire in the latter fluid.

The view has been presented that the granular elements found in *L* cultures represent protoplasmic debris[3]. As shown in Table 1, however, mechanically disintegrated *Proteus L9* bodies exhibit at the most a very low respiration. Thus, the granular bodies described above seem to be characterized by a higher structural organization than the dispersed protoplasm. The presence in the granules of succinic dehydrogenase, catalase and ribonucleic acid, in roughly similar amounts per mgm. dry weight as in *L* bodies not subjected to differential centrifugation, is also worth mentioning in this connexion.

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GENETICS

Relation between X-Ray Sensitivity and Cell Stages in Males of *Drosophila melanogaster*

Lüning[1] has shown that the rate of dominant lethals and gross rearrangements varies with the time from irradiation to insemination, with a peak around 7–10 days after the treatment. He suggests that the peak corresponds to irradiated spermatids which hence are supposed to be more sensitive than mature sperm. Auerbach[2] claims that the sensitive stage, although it may include late meiosis, consists mainly of spermatid stages. Khishin[3], comparing the mutation pattern from irradiation of larvæ, pre-pupæ and pupæ, agrees with Auerbach. Fritz-Niggli[4] adopted the same technique and deduced by analogy the following pattern of time-lapse between irradiated stages and insemination: mature sperm the 1st–4th day; spermatids the 4th–7th day; meiosis the 7th–10th day; and from the 10th day after irradiation spermatogonia.

The present investigation is an attempt to find the time of the appearance of the sperm irradiated in

meiosis by a direct method, and at the same time to correlate this with the sensitivity pattern. Mavor[5,6] showed that irradiation of females caused primary nondisjunction. The same ought to be true also in males if meiotic stages are irradiated. The appearance of individuals in which the paternal sex-chromosomes both have entered the sperm cell will indicate that the cell had been treated before anaphase I. In the present experiment the occurrence of *XO* males has been used as an indication of genetical damage. At the same time the induction of nondisjunction between the *X* and *Y* chromosomes in the males has served as a criterion of early meiosis (prior to anaphase I).

The following stocks were used: the females were taken from a *y w sn* ♀♀ × *y w sn*; *sc*^{8}*Y* ♂♂ stock and the males from a *y*^{16} ♀♀ × *y*^{16}; *sc*^{8}*Y* ♂♂ stock. The normal offspring would be *y* females and *w sn* males. Individuals which had lost the *X* and/or *sc*^{8}*Y*, and consequently were *XO*, would phenotypically be *y w sn*; and eggs fertilized by an *X*; *sc*^{8}*Y* carrying sperm (nondisjunction) would give wild-type females due to the presence of the *y*$^{+}$ locus in the *Y* chromosome (*y w sn*; *y*^{16}; *sc*^{8}*Y*). As these females also may arise through induced crossing-over between the *X* and the *Y* chromosome, each wild-type female was tested individually. The majority of these were due to nondisjunction. The males were picked out when 0–1 day old. They were either irradiated when they had woken up after treatment with ether or kept without females for 3 days prior to irradiation. The males were irradiated with a dose of 1,100 r. (2 min.). Immediately after irradiation the males were transferred to a mating box. The first mating period lasted 4 hr., but from the 4th day onwards each period consisted of 24 hr. Between the first mating period and the 4th day the males were kept with an excess of females.

Table 1. 0–1-day and 3–4-day-old *y*^{16}; *sc*^{8}*Y* Males were given 1,100 r. in Air and were then mated to *y w sn* Females. Total Number of Offspring as well as Rate of *XO* Males and Wild-type Females are Given

Mating period after irradiation	0–1-day-old males			3–4-day-old males		
	Percentage *XO* ♂♂	Percentage wild type ♀♀	Total offspring	Percentage *XO* ♂♂	Percentage wild type ♀♀	Total offspring
0–4 hr.	0·46	0·01	20,538	0·32	0·03	44,635
Fourth day	0·33	0·03	62,692	0·20	0·04	43,016
Fifth day	0·75	0·03	50,552	0·43	0·02	38,766
Sixth day	1·33	0·01	24,735	0·61	0·02	17,571
Seventh day	2·21	0·22	18,100	1·24	0·12	14,155
Eighth day	3·47	0·51	13,350	1·55	0·21	11,706
Ninth day	2·39	0·19	7,772	0·96	0·13	8,724
Tenth day	0·54	0·18	27,946	0·49	0·14	8,312
Eleventh day	0·46	0·14	30,044	0·19	0·05	7,807

From Table 1, which shows the results after irradiation of 0–1-day- and 3–4-day-old males, it can be seen that, independent of the age of the males at time of irradiation, the number of induced *XO* males rises steeply from the 4th day, reaching a peak on the 8th day after treatment and then decreasing towards the 11th day. As regards the frequency of induced wild-type females, the rate is practically unchanged from the first mating period until the 6th day after irradiation. On the 7th day after irradiation there is a sharp increase in the frequency of wild-type females. The frequency reaches a peak during the 8th day after irradiation, followed by a drop towards the 11th day.

It is of special interest to compare the frequency of induced *XO* males and the rate of induced nondisjunction females during the 4th–10th day after irradiation. It can be seen that the peak of *XO* males coincides with the peak of nondisjunction females. Since the occurrence of nondisjunction females is used as the criterion of early meiosis (prior to anaphase I) there is an agreement between the highest X-ray sensitivity and cells treated at early meiotic stages.

About the same sensitivity pattern is obtained after irradiation of 0–1 and 3–4 day old males respectively. There exists, however, a discrepancy in the amplitude of the sensitivity. The frequency of induced *XO* males, as well as the rate of induced nondisjunction females, is much lower in the experiments with 3–4 day old males. This difference is statistically significant except for the first mating period. There is a fairly good agreement between these findings and Lüning's[1] conclusions that 6–7-day-old males vary much less than 0–1-day-old males between different stages of spermiogenesis.

These experiments show that the treated meiotic cells become available for insemination during the 7th day after irradiation and onwards. From the present material it can be concluded that the peak of sensitivity presumably corresponds to cells treated during metaphase I or before anaphase I is completed. This conclusion is supported by sensitivity studies performed on different material[7–10].

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VIROLOGY

Virus Survival as a Seasonal Factor in Influenza and Poliomyelitis

The pronounced seasonal fluctuations in the morbidity of influenza and poliomyelitis are largely unexplained. Both diseases can probably be transmitted by airborne infection and by many other ways which involve the survival of the causative virus in the dry state. For many organisms survival in air can be taken as indicator for survival in the dry state in general. Consequently it seemed worth while to study the influence of temperature and humidity on the survival of the viruses of influenza and poliomyelitis in air.

Earlier experiments with aerosols[1] of many organisms showed that—at least in the range of indoor temperature—the influence of temperature is small (Q_{10} = 2–3) compared with the influence of humidity. Furthermore it became evident that the relative humidity and not the absolute humidity is the determining factor.

Both viruses were aerosolized for 2 min. with an indirect spray (mean droplet diameter 6μ) into a

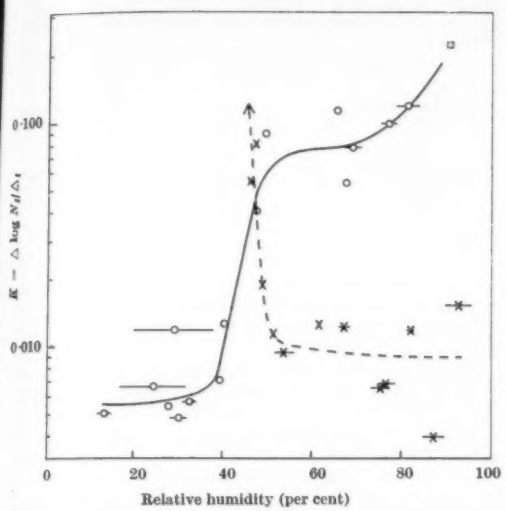

Fig. 1. Death-rates for influenza virus (○) and poliomyelitis virus (×) in air plotted against relative humidity

static system (4 M^1). Influenza virus (PR_8) was suspended in one part allantoic fluid and one part 2 per cent Difco peptone. Poliomyelitis virus (type 1 *CSl*) was suspended in one part Hanks salt solution with lactalbumin-hydrolysate and 5 per cent horse serum and one part peptone. At various times samples were taken for 2 min. with modified capillary impingers containing 1 per cent peptone or 1 per cent peptone with Dulbecco buffer.

Virus was titrated by amnion inoculation for influenza and by the plaque method on human amnion cells (strain *U*) for polio-virus.

From the logarithmic phase of the inactivation curves at various relative humidities, death-rate constants were calculated, using $K_2 = \Delta \log N_t/\Delta_t$ (t denoting time in minutes). K is plotted against relative humidity in Fig. 1. For influenza virus the death-rate is high (0·091 ± 0·024) at 50–90 per cent relative humidity and low (0·0073 ± 0·0031) in the range 15–40 per cent relative humidity. The transition is rather sharp. These results are mainly in accordance with the limited experiments published previously by other authors[2–6]. For poliomyelitis the inverse is true. Inactivation is slow (K = 0·0089 ± 0·0036) at high relative humidity and very fast at low relative humidity. In fact, below 45 per cent no virus could be detected 30 sec. after spraying, which means that less than 0·03 per cent of the virus was left. The transition is again sharp.

In temperate climates influenza generally is a winter disease, occurring during the period when the relative humidity indoors is low as a result of heating. In Fig. 2 the seasonal variation of indoor humidity is plotted. The period of increasing influenza morbidity coincides with the period during which the survival of the virus in air is optimal.

Increase of poliomyelitis morbidity occurs during summer, that is, during the period when the indoor relative humidity is optimal for the survival of the virus in air (and presumably in the dry state in general).

Consequently the relative humidity, indoors, is considered as an important environmental factor contributing to the seasonal fluctuations of the morbidity of these two virus diseases.

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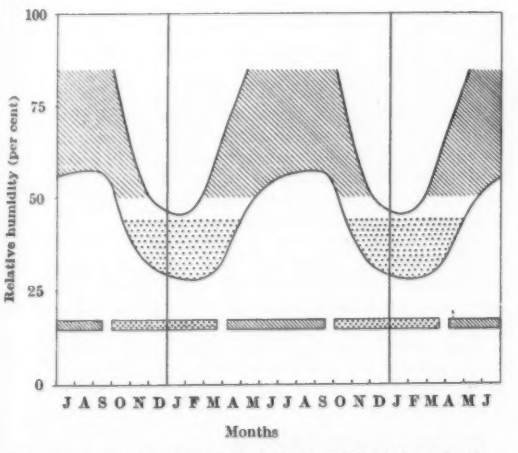

Fig. 2. Seasonal variation of relative humidity indoors in the Netherlands. The upper and lower curves represent mean maximal and minimal relative humidity as calculated from temperature and absolute humidity. The range for optimal virus-survival is stippled for influenza virus and hatched for polio virus. The period of increasing morbidity of influenza (data for England and Wales) and for poliomyelitis (Dutch data) are given at the bottom of the figure as stippled and hatched bars

Association of *Olpidium brassicae* and Tobacco Necrosis Virus

Tobacco necrosis virus infects the roots of many plants, usually without symptoms. The virus is soil-borne[1–3], but the conditions necessary for natural infection have not been determined. Attempts to obtain artificial infection of roots by adding virus suspensions to roots of plants grown in sterilized soil commonly fail.

The relationship of *Olpidium brassicae* to tobacco necrosis virus infection was investigated because of claims[4–7] of an association between tobacco necrosis virus and lettuce big vein disease, with which *O. brassicae* is invariably associated[8,9].

Further circumstantial evidence for the association of tobacco necrosis virus and *O. brassicae* was obtained in the present work by microscopic detection of *Olpidium* in the roots of *Cleome spinosa*, *Fragaria vesca*, *Chenopodium amaranticolor*, tobacco, and French bean infected with tobacco necrosis virus.

When suspensions of *Olpidium* zoospores from lettuce plants shown by root assay to be free of tobacco necrosis virus, and suspensions from macerated virus-infected cowpea leaves were simultaneously watered on to potted lettuce seedlings, much greater

Table 1. AVERAGE NUMBERS OF TOBACCO NECROSIS VIRUS LESIONS PER ASSAYED PLANT FROM INOCULATION OF LETTUCE ROOTS WITH *Olpidium brassicae* AND TOBACCO NECROSIS VIRUS

Treatment	Total number of plants assayed	Total number of plants infected with virus	Average number of virus lesions per plant assayed
Olpidium + virus	40	38	36·7
Virus only	31	17	0·7
Olpidium only	20	3	0·1*
Nil	14	1	0·1*

* Infection probably resulting from contamination.

root infection by tobacco necrosis virus occurred than when the virus alone was applied. Results in three experiments are summarized in Table 1.

Similar results were secured when cowpea, French bean, cabbage, cucumber, and tobacco were inoculated with *Olpidium* and tobacco necrosis virus. The results have been repeated in water culture in the laboratory with seedlings raised in Petri dishes.

The mode of action of *Olpidium* zoospore suspensions in thus increasing root infection with tobacco necrosis virus is not known. Conceivably, the fungus may act as a virus vector or it may predispose the roots to infection. Zoospore suspensions from lettuce roots infected with both *Olpidium* and tobacco necrosis virus have caused virus infection of roots even without added virus. As tobacco necrosis virus is released naturally by infected roots[10], however, this does not necessarily mean that *Olpidium* is acting as a virus vector.

It is possible, but unlikely, that some factor other than *Olpidium* obtained from lettuce roots is responsible for the increased virus infection; a final decision on this must wait until it becomes possible to grow *Olpidium* in pure culture.

The advice of C. E. Yarwood and R. G. Grogan is gratefully acknowledged. C. E. Yarwood, N. W. Frazier, and T. Bowman kindly furnished plants naturally infected with tobacco necrosis virus.

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AGRICULTURE

Contribution of Rainwater to the Nutrient Economy of Soil in Northern Nigeria

THE contribution of rainwater to the nutrient economy of soil in many regions of the world has been studied. At Samaru, Northern Nigeria, 80 litres of rainwater from eight rain gauges were collected in 1959. The water was concentrated by evaporation from dilute sulphuric acid and the concentrate analysed for all major nutrients except sulphur. Forty-two inches of rain fell during the 1959 season. The results are expressed in p.p.m. of each element in the total composite sample, and have been converted to pounds per acre (Table 1). Sampling procedure excluded any measure of seasonal distribution.

Table 1. NUTRIENT CONTRIBUTION OF RAINWATER IN 1959 AT SAMARU, NORTHERN NIGERIA

Nutrient	p.p.m.	lb./acre
Nitrogen		
Ammonium	5·000	47·6
Nitrate	0·230	1·2
Organic	0·125	2·0
Total	5·355	50·8
Phosphorus	0·555	2·3
Potassium	3·500	32·8
Calcium	0·100	0·9
Magnesium	0·110	2·60
Sodium	5·750	53·8

So far as I am aware, the nitrogen, potassium and sodium figures are the highest recorded. Despite the high values, the sodium/potassium ratio is of the order found in New Zealand by Wilson[1]. He has shown that the nutrients present in snow originate from the surface of the ocean where a large number of plankton, etc., in various stages of growth and decomposition are concentrated. These organisms narrow down the potassium/sodium ratio of the underlying sea. The potassium/sodium ratio of sea-water is 1 : 27, snow-water in New Zealand showed a ratio of 1 : 2·7 and at Samaru a ratio of 1 : 1·6 was found. The narrower ratio at Samaru may be due to a higher or different biological activity in the warm ocean around West Africa compared with New Zealand conditions. The low nitrate figure eliminates the possibility of large contributions from dust and electric storms. The lack of seasonal distribution figures makes the evaluation of the various factors impossible. Generally, the figures to date point to the ocean as the main source of rainwater nutrients, but do not exclude contributions from other factors.

The presence of such large and varied quantities of nutrients in the rainwater helps to explain several aspects of soil fertility in Northern Nigeria.

(1) Potassium fertilizers have never shown a positive response on annual crops of the region. Potassium from rainwater is probably adequate for crop growth, and the fertilizer potash aggravates what must be already an imbalance of potassium to other nutrients.

(2) Despite the lack of leguminous plants in bush fallows, build up of organic nitrogen is appreciable. From unpublished soil analysis data at Samaru, it has been calculated that an increase of 0·025–0·03 per cent total nitrogen can be expected over a period of five years. Rainwater, if not lost by run-off, would contribute 0·013 per cent nitrogen.

(3) Light sandy soils in the extreme north of the region show very low levels of total nutrients, and crop growth would seem to be impossible. The contribution of rainwater helps to explain the growth of crops on these soils.

These results indicate the importance of rainwater as a source of nutrients in the soil of Northern Nigeria. More detailed studies are in progress.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, October 31

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE (in the Council Room (second floor) of the Science Museum, Exhibition Road, London, S.W.7), at 5.30 p.m.—Prof. Benjamin Farrington: "Francis Bacon at the Crossroads".

INSTITUTION OF MECHANICAL ENGINEERS, APPLIED MECHANICS and LUBRICATION GROUPS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Rolling Bearing Problems—Is There a Need for Fundamental Research?".

INSTITUTION OF THE RUBBER INDUSTRY (at the Café Royal, 68 Regent Street, London, W.1), at 6 p.m.—Mr. E. B. Storey: "Estimation of Wear Resistance of Tread Vulcanizates".

Tuesday, November 1

UNIVERSITY OF LONDON (at the Middlesex Hospital Medical School, Mortimer Street, London, W.1), at 5.15 p.m.—Prof. Hans Schaefer (University of Heidelberg): "Principles of Circulatory Regulation".*

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. G. G. Haigh: "Transistor Instrumentation in Rockets".

UNIVERSITY OF LONDON (at the Imperial College of Science and Technology, London, S.W.7), at 5.30 p.m.—Prof. K. G. Denbigh: "The Science of Continuously Operating Systems" (Inaugural Lecture).

Wednesday, November 2

SOCIETY FOR ANALYTICAL CHEMISTRY (at the Wellcome Building, Euston Road, London, N.W.1), at 2 p.m.—Meeting on "Analysis of Semi-Conductors".

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Prof. R. H. S. Thompson: "Biochemistry of Multiple Sclerosis".*

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. M. J. Rickard: "The Stratigraphy and Structure of the Errigal Area, Co. Donegal"; Dr. B. A. Sturt: "The Geological Structure of the Area South of Loch Tummel".

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Mr. J. Tubman and Mr. J. F. Manger: "Applied Petroleum Research on a Vehicle Dynamometer".

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. W. J. G. Beynon: "The Ionosphere—a Review of Recent Progress".

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5.30 p.m.—Dr. A. W. Brewer: "The Stratosphere".

INSTITUTION OF MECHANICAL ENGINEERS, INTERNAL COMBUSTION ENGINE GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "The Days of the Diesel Engine are Numbered".

BRITISH INSTITUTION OF RADIO ENGINEERS, RADAR GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—"Radar—Pulse or C.W.?" (a Discussion on Relative Merits).

SOCIETY FOR VISITING SCIENTISTS (at 5 Old Burlington Street, London, W.1), at 7.30 p.m.—Discussion Meeting on "Noise". Chairman: Sir Gordon Sutherland, F.R.S. Speakers: Mr. D. W. Robinson, Prof. W. Burns and Dr. A. Carpenter.

Thursday, November 3

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Dr. A. M. Lwoff, For.Mem.R.S.: "Viral Functions" (The Leeuwenhoek Lecture).

MINERALOGICAL SOCIETY (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Scientific Papers (Anniversary Meeting).

UNIVERSITY OF LONDON (at Wye College, Wye, Ashford, Kent), at 5 p.m.—Dr. J. T. Martin: "The Plant Cuticle: Its Structure and Relation to Spraying Problems".*

UNIVERSITY OF LONDON (at the Middlesex Hospital Medical School, Mortimer Street, London, W.1), at 5.15 p.m.—Prof. Hans Schaefer (University of Heidelberg): "The Theory and Interpretation of the Electrocardiogram".*

INSTITUTION OF ELECTRICAL ENGINEERS (joint meeting with the INSTITUTIONS OF CIVIL and of MECHANICAL ENGINEERS, at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. W. Abbott: "The Training of Oversea Graduate Engineers, with particular reference to the F.B.I. Scholarships Scheme".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. Charles Wilcocks: "Aspects of Medical Investigation in Africa—Schistosomiasis".* (Second of four Heath Clark Lectures. Further lectures on November 9 and 10.)

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. K. M. Rudall: "Regular Folds in Protein and Polysaccharide Chains".* (Fifth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

ARTHUR STANLEY EDDINGTON MEMORIAL TRUST (at Friends House, Euston Road, London, N.W.1), at 6 p.m.—Dr. William H. Thorpe, F.R.S.: "Biology, Psychology and Belief" (Fourteenth Eddington Memorial Lecture).

INSTITUTE OF METALS, LONDON LOCAL SECTION (at the Royal School of Mines, Prince Consort Road, London, S.W.7), at 7 p.m.—Dr. N. P. Allen, F.R.S.: "Long Term Creep Tests: a Discussion of Recently Expressed Views".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the BRUNEL COLLEGE OF TECHNOLOGY CHEMICAL SOCIETY, at the Brunel College of Technology, Woodlands Road, London, W.3), at 7 p.m.—Dr. C. C. Addison: "Non-aqueous Solvent Systems".

CHEMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 7.30 p.m.—Scientific Papers.

Friday, November 4

MINERALOGICAL SOCIETY, CLAY MINERALS GROUP (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 10.45 a.m.—Autumn Meeting.

UNIVERSITY OF LONDON (at the Institute of Obstetrics and Gynæcology, Chelsea Hospital for Women, Dovehouse Street, London, S.W.3), at 3 p.m.—Prof. E. C. Amoroso: "The Endocrinology of Pregnancy".*

CIBA FOUNDATION FOR THE PROMOTION OF INTERNATIONAL CO-OPERATION IN MEDICAL AND CHEMICAL RESEARCH (at the Royal Institute of British Architects, 66 Portland Place, London, W.1), at 5 p.m.—Prof. J. Konorski (Warsaw): "Changing Concepts Concerning Physiological Mechanisms of Animal Motor Behaviour" (Twelfth (Annual) Ciba Foundation Lecture).

INSTITUTION OF ELECTRICAL ENGINEERS, MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Electro-Convulsive Therapy" opened by Dr. A. Spencer-Patterson and Mr. W. H. Stanton.

SOCIETY OF DYERS AND COLOURISTS, LONDON SECTION (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 6 p.m.—Mr. A. J. Lenz: "Fastness of Dyes and Finishes".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. G. Porter: "Very Fast Chemical Reactions".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

EXPERIMENTAL OFFICER (at least 26, with a pass degree or equivalent, experience in radiochemistry and the use of normal beta counting equipment, and preferably a working knowledge of alpha and gamma counters), for work involving the measurement of radioactivity in biological materials—The Director, Agricultural Research Council, Biological Laboratory, Letcombe Regis, Wantage, Berks (November 2).

BIOCHEMIST (non-medical), for research on problems connected with tropical diseases—The Secretary, Hospital for Tropical Diseases, 4 St. Pancras Way, London, N.W.1 (November 5).

LABORATORY TECHNICIAN (qualified, with experience of laboratory work) at Brentwood Teacher Training College—Chief Education Officer (Ref. F.5.k), County Offices, Chelmsford (November 5).

RESEARCH ASSISTANT IN THE DEPARTMENT OF BOTANY, to carry out research with Dr. L. Fowden on nitrogen metabolism—The Secretary, University College, Gower Street, London, W.C.1 (November 7).

HEAD (with high qualifications and experience) OF THE DEPARTMENT OF PHYSICS—The Bursar, College of Advanced Technology, Gosta Green, Birmingham 4 (November 8).

LECTURER (with medical qualifications registrable in this country) IN PSYCHIATRY—The Registrar, The University, Manchester 13 (November 12).

CHAIR OF PHYSICS in the University of Khartoum—The Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 15).

LECTURER or ASSISTANT LECTURER (with special qualifications in applied mathematics) IN THE DEPARTMENT OF MATHEMATICS of the Faculty of Science—The Registrar, The University, Manchester 13 (November 16).

EXPERIMENTAL AND THEORETICAL PHYSICISTS (with a first- or second-class honours degree in physics or mathematics), for research work in the Reactor Development Division—Personnel Branch (W.348/34), U.K.A.E.A., Atomic Energy Establishment, Winfrith, Dorchester, Dorset (November 17).

LECTURER (with a science degree with zoology as a major subject, followed by postgraduate experience leading to a higher degree and/or to published work) IN ZOOLOGY in the University College of Townsville, University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 19).

LECTURER (with a degree in science with honours in physics, some experience in the use of ionizing radiation, and preferably experience in using radioactive substances and in the principles of hospital or health physics) IN RADIATION PHYSICS AND RADIATION SAFETY OFFICER at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, November 19).

LECTURER or ASSISTANT LECTURER (with a special interest in plant physiology) IN BOTANY at the University College of Rhodesia and Nyasaland—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (November 30).

SENIOR LECTURER or LECTURER (with an honours degree or equivalent qualifications, and industrial and/or research experience) IN STRUCTURAL ENGINEERING—The Registrar, Bristol College of Science and Technology, Ashley Down, Bristol 7 (December 3).

LECTURER IN BIOCHEMISTRY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 5).

PLANT PHYSIOLOGIST (with a good honours degree in botany and research experience), for investigation of effects of temperature, oxygen and carbon dioxide on the respiration of apples—The Director, Ditton Laboratory, Agricultural Research Council, Larkfield, Maidstone, Kent (December 10).

SENIOR LECTURER IN PHILOSOPHY at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, December 10).

EMPIRE RHEUMATISM COUNCIL FELLOW (with medical or scientific qualifications), to prosecute research in the field of rheumatism—The General Secretary, Empire Rheumatism Council, Faraday House, 8/10 Charing Cross Road, London, W.C.2 (December 15).

AGRICULTURAL OFFICER (TOBACCO RESEARCH) (with a good honours degree in natural science (botany), or a degree in horticulture, with suitable postgraduate training or experience) in Nyasaland, for experimental work on tobacco including agronomy trials and plant breeding—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/4/04.

ASSISTANT, Grade B (with a university degree and preferably some teaching experience), TO TEACH BOTANY AND ZOOLOGY to Advanced Level students—The Clerk to the Governors, South-West Essex Technical College and School of Art, Forest Road, Walthamstow, London, E.17.

ASSISTANT PROFESSORS, INSTRUCTORS or LECTURERS (2) (with the degree of Ph.D.) IN PHYSICS, to direct experimental research in low temperature or solid state physics—The Chairman, Department of Physics, Western Reserve University, Cleveland 6, Ohio, U.S.A.

CLAY MINERALOGIST (with an appropriate academic background and experience) IN THE DEPARTMENT OF MINES AND TECHNICAL SURVEYS, Canada, for research aimed at the development of useful properties in Canadian clays and shales—Dept. MTS 1518, National Employment Service of Canada, 61 Green Street, London, W.1.

GRADUATE RESEARCH ASSISTANT IN THE DEPARTMENT OF PHYSICS, for a study of crystal structure and texture of materials by the techniques of electron diffraction and microscopy leading if desired to a higher degree—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1.

LECTURER IN THE DEPARTMENT OF PHYSICS—The Principal, Huddersfield College of Technology, Huddersfield.

LECTURER (with marked ability at conducting and supervising research) IN THE CHEMICAL PHYSICS OF SOLIDS—Prof. A. R. Ubbelohde, F.R.S., Department of Chemical Engineering and Chemical Technology, Imperial College of Science and Technology, London, S.W.7.

MASTER TO TEACH PHYSICS (the post involves some Sixth Form work)—The Headmaster, King's College School, Wimbledon, London, S.W.19.

RESEARCH ASSOCIATE IN ORGANIC CHEMISTRY, for work involving the isolation and identification of products formed by action of gamma radiation or organic compounds (mainly amines)—The Professor of Organic Chemistry, King's College (University of Durham), Newcastle upon Tyne 1.

RESEARCH FELLOWS and RESEARCH ASSISTANTS (4) IN THE DEPARTMENT OF PHARMACY—The Registrar, Bradford Institute of Technology, Bradford 7.

SENIOR LECTURER or LECTURER (with a first- or second-class honours degree and a thorough grounding in electronics, and preferably experience in radar, telecommunications or radio guidance of missiles) IN ELECTRONICS at the Royal Military College of Science, Shrivenham, Berkshire—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting D.690/0A.

TECHNICAL OFFICER (preferably with workshop and electronics experience), for research in muscle biophysics, using the electron microscope, X-ray diffraction, etc.—The Director, Medical Research Council Biophysics Research Unit, King's College, Strand, London, W.C.2.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Colour Filmstrips on Soil. No. 1: Rocks and Erosion. 38 frames. Notes. Pp. 14. No. 2: Plants and Decay. 35 frames. Notes. Pp. 16. No. 3: Soil Profiles and Their Information. 37 frames. Notes. Pp.12. No. 4: Composition of Soil. 35 frames. Notes. Pp. 17. No. 5: Soil and Farming. 37 frames. Notes. Pp. 26. (Surbiton: Marian Ray, 36 Villiers Avenue, 1960.)

The Morgan Crucible Company Limited. The Chairman's speech at the 26th Annual General Meeting held at Battersea Works on Thursday, 28th July, 1960. Pp. 4. (London: The Morgan Crucible Company, 1960.) [28

Ministry of Agriculture, Fisheries and Food. At the Farmers' Service: a Handy Reference to various services available to Farmers in England and Wales. Pp. 81. (Kew, Surrey: Ministry of Agriculture, Fisheries and Food (Publications), 1960.) [28

Freshwater Biological Association. Twenty-eighth Annual Report for the year ended 31 March 1960, including Reports of the Council and of the Director, and Accounts for 1959–60, with Lists of Officers, Council, Staff and Members. Pp. 93. (Ambleside: Freshwater Biological Association, 1960.) [28

Beecham Group Journal, Vol. 1, No. 1 (Summer, 1960). Pp. 22. (Brentford, Mddx.: Beecham Group Ltd., 1960.) [28

Department of Scientific and Industrial Research. Report of the Tropical Products Institute 1959: The Report of the Tropical Products Institute Committee, with the Report of the Director of the Tropical Products Institute. Pp. iv+40. (London: H.M. Stationery Office, 1960.) 2s. 6d. net. [28

Philosophical Transactions of the Royal Society of London. Series A: Mathematical and Physical Sciences. No. 1020, Vol. 253 (28 July 1960): Stability of Flow in a Rotating Viscous Incompressible Fluid Subjected to Differential Heating. Pp. 1–25. 8s. No. 1021, Vol. 253 (28 July 1960): Hassitt-Type Young Operator Expansions, 1: An Orthogonal Transformation between (a) the Young Operators of the Symmetric Group S_A+1 and (b) the Two-Sided Products of the Young Operators of S_A with the Transposition P_A, $A+1$. By H. A. Jahn. Pp. 27–53. 8s. 6d. (London: The Royal Society, 1960.) [28

Other Countries

Parapsychology Foundation, Inc., New York. Parapsychological Monographs No. 2: ESP in Relation to Rorschach Test Evaluation. By Gertrude Schmeidler. Pp. iii+89. (New York: Parapsychology Foundation, Inc., 1960.) [28

Louisiana Agricultural Experiment Station. Southern Co-operative Series. Bulletin No. 63: Summer Climate and Its Effects on Dairy Cattle in the Southern Region. Pp. 63. (Baton Rouge, Louisiana: Louisiana Agricultural Experiment Station, 1959.) [28

Chicago Natural History Museum. Fieldiana: Geology. Vol. 11, No. 10: Fishes of the Devonian Holland Quarry Shale of Ohio. By Robert H. Denison. Pp. ii+555–613. 1.50 dollars. Vol. 14, No. 1: The Stratigraphy of the Devonian Holland Quarry Shale of Ohio. By J. Ernest Carman. Pp. 5. 15 cents. Fieldiana: Zoology. Vol. 39, No. 35: Two Eels of the Genus *Synaphobranchus* from the Gulf of Mexico. By P. H. J. Castle. Pp. 387–398. 30 cents. Vol. 39, No. 36: A New Genus of Blind Beetles from a Cave in South Africa. By Henry S. Dybas. Pp. 399–405. 20 cents. (Chicago Natural History Museum, 1960.) [28

United States Department of the Interior: Fish and Wildlife Service. Fishery Bulletin No. 172: Seasonal Abundance and Vertical Movements of Planktonic Crustacea in Lake Michigan. By LaRue Wells. Pp. iv+343–369. (Washington, D.C.: Government Printing Office, 1960.) 25 cents. [28

Smithsonian Institution. Proceedings of the United States National Museum. Vol. 112, No. 3431: Lace-Bug Genera of the World (Hemiptera: Tingidae). By Carl J. Drake and Florence A. Ruhoff. Pp. 1–105. Vol. 112, No. 3432: Flies of the Family Conopodae from Eastern Asia. By Sidney Camras. Pp. 107–131. Vol. 112, No. 3433: Fireflies of the Genus *Pyractonema* (Coleoptera: Lampyridae). By Frank A. McDermott. Pp. 133–157. Vol. 112, No. 3434: North and South American Copepods of the Genus *Hemicyclops* (Cyclopoida: Clausididae). By Richard U. Gooding. Pp. 159–195. Vol. 112, No. 3435: Chironomid Midges of California. 1: Chironominae, exclusive of Tanytarsini (=Calopsectrini). By James E. Sublette. Pp. 197–226. (Washington, D.C.: Government Printing Office, 1960.) [28

Pacific Marine Fisheries Commission. Bulletin No. 4: A Study of Annual and Seasonal Bathymetric Catch Patterns for Commercially Important Groundfishes of the Pacific Northwest Coast of North America. By Dayton L. Alverson. Pp. ii+66. (Portland, Oregon: Pacific Marine Fisheries Commission, 1960.) [28

United States Department of Health, Education and Welfare. Public Health Service Publication No. 761: Activities of the National Institute of Health in the Field of Gerontology—Research Grant and Training Projects active on January 31, 1960, and Intramural Research Projects carried on during calendar year 1959. Pp. v+41. (Washington, D.C.: Government Printing Office, 1960.) 30 cents. [28

United States Department of Commerce: Coast and Geodetic Survey Technical Bulletin No. 11: Use of Near-Earth Satellite Orbits for Geodetic Information. By Paul D. Thomas. Pp. ii+36. (Washington, D.C.: Government Printing Office, 1960.) 45 cents. [28

Monatsberichte der Deutschen Akademie der Wissenschaften zu Berlin. Band 1, Heft 1. Herausgegeben im Auftrage der Deutschen Akademie der Wissenschaften zu Berlin von G. Rienäcker. Pp. 1–30. (Berlin: Akademie-Verlag, 1959.) [28

The Annual of Czechoslovak Medical Literature, 1957. By Státní Lékarská Knihovna. Pp. xxi+509. (Praha: Státní Zdravotnické Nakladatelstvi, 1959.) [28

United States Department of Agriculture. Leaflet No. 474: Chicken Lice: How to Control Them. Pp. 8. (Washington, D.C.: Government Printing Office, 1960.) 5 cents. [28

World Meteorological Organization: The First Ten Years. Pp. 32. (Geneva: World Meteorological Organization, 1960.) [28

A Study of Air Pollution: Diffusion and Sampling. By Dr. L. A. Clarenburg. (Doctoral Thesis.) Pp. xi+89. (Utrecht: Drukkerij Schotanus and Jens, 1960.) [28

Smithsonian Miscellaneous Collections. Vol. 140, No. 2: Pleistocene Birds in Bermuda. By Alexander Wetmore. Pp. i+11+3 plates. (Publication No. 4423). (Washington, D.C.: Smithsonian Institution, 1960.) [28

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